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THE EFFECTS OF AFFERENT CIRCULATORY ARREST UPON HYDROGEN ION CONCENTRATION OF THE LIVER

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CONTROL OF MAJOR HEMORRHAGE is always a matter of grave concern in the surgical treatment of hepatic lesions. The formidable proportions of blood loss incident to elective liver resection are reflected in the large amounts of blood necessitated for replacement during these procedures. Shock resulting from hemorrhage is practically always the leading cause of death in any series of cases which is concerned with liver wounds.

The problem is further complicated by the intolerance of the liver to long periods of temporary afferent vascular occlusion. Raffucci found this to be fatal in 49 of 50 dogs subjected to occlusion of the hepatic artery and portal vein for 1 hour. The cause of death under these circumstances has not as yet been clearly defined.

This study was undertaken to record the *p*H of the normal liver, along with any alteration of this value that might result from occlusion of the hepatic artery and portal vein separately and simultaneously.

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Aided by United States Public Health Service, Grant RG-4745.

MATERIALS AND METHODS

Twenty-five randomly selected adult mongrel dogs were used for these experiments. Anesthesia was induced and maintained with fractional, intravenous doses of nembutal. Exposure of the liver was accomplished through an upper midline abdominal incision.

Measurement of liver tissue pH. A Beckman quinhydrone glass electrode constructed for tissue *p*H measurements was used for these determinations. After proper standardization with buffers ranging from *p*H 7.00 to 4.00, the tip of the electrode was inserted directly into the liver tissue to a depth of approximately ¼ inch. An ordinary calomel reference electrode was placed in the abdominal cavity. The electrodes were connected to a photovoltic direct reading, line operated *p*H meter (accuracy of ±0.05 *p*H units). The *p*H apparatus was restandardized at regular intervals, and corrections were made for temperature differences. The indicating electrode was allowed to remain in the liver throughout an entire experiment except during standardizations of the system. Over-all accuracy of the *p*H indicating

TABLE I.—HEPATIC *p*H VALUES WITH NORMAL CIRCULATION

Time (mins.)	Initial	5	10	15	20	25	30	35	40	45	50	55	60
Mean	7.28	7.15	7.10	7.07	7.07	7.06	7.06	7.06	7.05	7.05	7.05	7.05	7.06
Range	7.20	7.03	7.05	7.00	7.00	6.99	7.00	7.00	7.00	7.00	7.00	7.00	7.01
	7.45	7.35	7.21	7.12	7.18	7.10	7.10	7.12	7.13	7.11	7.11	7.10	7.11

TABLE II.—THE EFFECT OF PORTAL VEIN OCCLUSION UPON LIVER *p*H

	Normal circulation						*Portal vein occlusion*											
Time (mins.)	5	10	15	20	25	30	5	10	15	20	25	30	35	40	45	50	55	60
Mean	7.19	7.09	7.03	7.02	7.01	7.01	7.03	7.00	6.99	7.00	6.96	6.96	6.96	6.96	6.96	6.97	6.96	6.94
Range	7.10	7.00	7.00	7.00	7.00	7.00	7.00	7.00	6.98	6.98	6.92	6.91	6.91	6.91	6.91	6.91	6.91	6.91
	7.30	7.25	7.05	7.05	7.05	7.05	7.10	7.01	7.17	7.05	7.00	7.00	7.01	7.01	7.00	7.00	7.00	7.00

TABLE III.—THE EFFECT OF HEPATIC ARTERY OCCLUSION UPON LIVER *p*H

	Normal circulation				*Hepatic artery occluded*											
Time (mins.)	5	10	15	20	5	10	15	20	25	30	35	40	45	50	55	60
Mean	7.25	7.10	7.09	7.09	6.92	6.82	6.82	6.82	6.81	6.79	6.80	6.78	6.79	6.79	6.79	6.79
Range	7.20	7.03	7.02	7.01	6.59	6.49	6.52	6.52	6.52	6.51	6.51	6.51	6.51	6.51	6.50	6.50
	7.30	7.20	7.20	7.20	7.11	6.95	6.95	7.00	7.00	6.90	6.97	7.00	6.99	6.99	6.99	6.99

TABLE IV.—EFFECT OF PORTAL VEIN OCCLUSION UPON HEPATIC *p*H 1 HOUR AFTER OCCLUSION OF THE HEPATIC ARTERY

Time (mins.)	5	10	15	20	25	30	35	40	45	50	55	60
Mean	6.78	6.67	6.59	6.55	6.53	6.50	6.47	6.44	6.41	6.39	6.33	6.30
Range	6.50	6.50	6.40	6.39	6.39	6.38	6.31	6.30	6.28	6.25	6.25	6.20
	6.99	6.85	6.80	6.75	6.75	6.72	6.70	6.65	6.60	6.60	6.42	6.42

TABLE V.—EFFECT OF TOTAL HEPATIC AFFERENT VASCULAR OCCLUSION UPON LIVER *p*H

	Normal circulation		*Afferent vessels occluded*											
Time (mins.)	Initial	5	5	10	15	20	25	30	35	40	45	50	55	60
Mean	7.34	7.15	7.03	6.91	6.84	6.79	6.72	6.68	6.67	6.62	6.46	6.44	6.43	6.43
Range	7.31	7.00	6.90	6.82	6.75	6.70	6.60	6.60	6.55	6.50	5.80	5.80	5.80	5.80
	7.39	7.26	7.18	7.10	7.04	7.02	7.00	6.95	6.95	6.90	6.82	6.75	6.72	6.71

TABLE VI.— EFFECT OF RELEASE OF TOTAL HEPATIC AFFERENT VASCULAR OCCLUSION OF 1 HOUR'S DURATION UPON *p*H

Time (mins.)	5	10	15	20	25	30	35	40	45	50	55	60
Mean	6.71	6.77	6.85	6.90	6.94	6.99	7.00	7.00	7.03	7.05	7.05	7.00
Range	6.67	6.73	6.80	6.80	6.85	6.90	6.90	6.90	6.90	6.90	6.90	6.90
	6.75	6.81	6.97	7.01	7.03	7.10	7.10	7.11	7.20	7.23	7.19	7.05

system was ±0.06 *p*H units. The *p*H values were recorded at 5 minute intervals for the duration of each experiment.

Experimental procedure. The animals used for these studies were divided into the following groups:

Group 1 (10 animals).—Normal liver tissue hydrogen ion activity was recorded for 1 hour without alteration of the blood flow.

Group 2 (5 animals).—Normal liver *p*H was recorded for 30 minutes, following which the portal vein was occluded. The *p*H values were then observed for a period of 1 hour.

Group 3 (5 animals).—In this series normal liver *p*H was recorded for 15 minutes. The hepatic artery was then clamped for 1 hour, during which time *p*H changes were recorded. Effects of the additional occlusion of the portal vein were observed for a second 60 minute period.

Group 4 (5 animals).—A portacaval shunt was first constructed in order to divert all portal blood from the liver and yet allow the portal system to empty. The hepatic

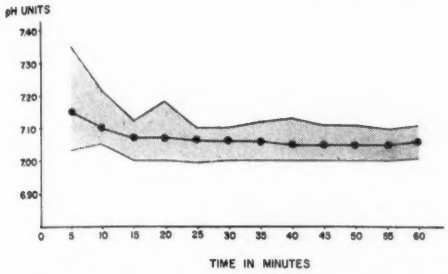

FIG. 1. Graph showing hepatic *p*H with normal circulation.

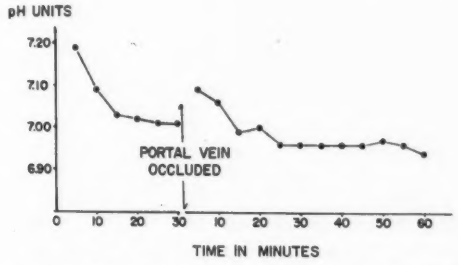

FIG. 2. Changes in liver *p*H resulting from portal vein occlusion.

artery was then clamped, producing "total" afferent circulatory occlusion of the liver for 1 hour. Hydrogen ion activity was recorded during this period of arrest and for 60 minutes following release of the occluding clamps.

RESULTS

Group 1. Introduction of the electrode into the liver without alteration of the circulation was followed by consistent *p*H changes for a short period of time (Fig. 1). The initial value is high and in each case approximates normal blood *p*H. The *p*H drops rapidly after electrode insertion, reaching a mean value of 7.10 after 10 minutes (Table I). Since the temperature of the electrodes and standard buffers was maintained at the same level as that of the liver, the initial *p*H value probably does not represent electrode equilibration.

Group 2. It is evident from Figure 2 that occlusion of the portal vein is followed by only slight alteration in liver *p*H under the conditions of this experiment. The mean *p*H values and the *p*H ranges subsequent to portal vein occlusion are presented in Table II.

Group 3. Occlusion of the hepatic artery distal to the gastroduodenal branch was followed by an average drop in *p*H to 6.82 after 10 minutes (Fig. 3). Any further drop in *p*H was gradual during the next 50 minutes as evidenced by a final mean reading of 6.79 (Table III). One hour after hepatic artery occlusion, the portal vein was also clamped. The liver *p*H began an immediate, precipitous fall, reaching a mean level of 6.50 after 30 minutes and 6.30 after 1 hour (Fig. 3, Table IV).

Group 4. All dogs in this group were Eck fistula animals. Both the hepatic artery and the portal vein were clamped simultane-

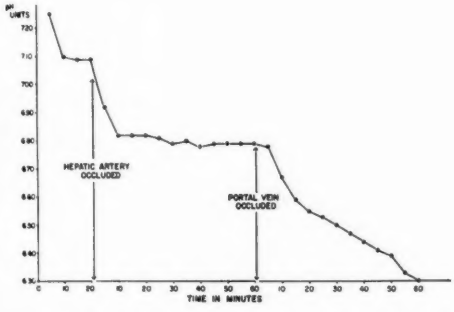

FIG. 3. Effects upon liver *p*H of hepatic artery and subsequent portal vein occlusion.

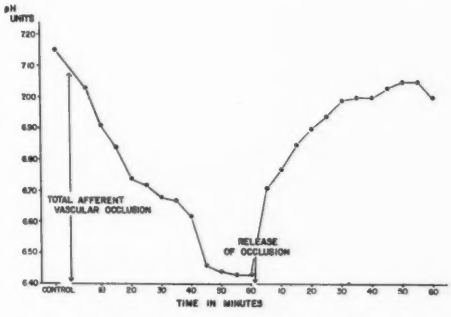

FIG. 4. Changes in liver *p*H resulting from afferent hepatic vascular arrest and release.

ously in this series. A rapid decline of *p*H to a mean value of 6.68 occurred 30 minutes following circulatory arrest to the liver. After 1 hour an average *p*H value of 6.43 was attained (Fig. 4, Table V). Removal of the occluding clamps from the hepatic artery and portal vein after 60 minutes resulted in a mean rise in *p*H to 6.71 in 5 minutes and to 7.00 within 1 hour (Table VI).

DISCUSSION

The *p*H time curve of the normal liver shows the initial reading to be much higher than subsequent values from the same tissue site (Fig. 1). This result apparently is due to bleeding following electrode insertion. If the indicating electrode is removed from one site and reinserted in a new position, another high reading will be obtained until bleeding ceases. Actually, less than 2 or 3 millimeters of blood are lost because of electrode puncture. The *p*H drops so that an equilibrium is reached approximately 10 minutes after placement of the indicating electrode. Caldwell has shown intracellular *p*H to be much lower (approximately 6.80 to 6.90) than that of the blood. It is probable, therefore, that the hydrogen ion activity as determined in this present study represents a value which results from a mixture of blood and extracellular and intracellular fluid.

The results indicate that the normal liver "tissue" of dogs has a *p*H value of about 7.06 as determined under the described conditions. Occlusion of the portal vein has no marked effect upon liver tissue *p*H, thus indicating that hepatic artery flow is sufficient to maintain the liver at a relatively normal *p*H. This finding is consistent with clinical evidence of no marked ill effects resulting from diversion of portal vein blood flow from the liver.

Arrest of the hepatic artery with a patent portal vein resulted in a fall of *p*H from a mean of 7.09 to 6.79 after 30 minutes, at which point it was consistently maintained. Portal vein blood flow, therefore, is not sufficient to maintain liver *p*H within the normal range. Apparently, if normal tissue hydrogen ion activity is to be maintained, the circulation must perform the dual function of supplying sufficient oxygen and removing metabolic end products. Hepatic artery flow appears to be capable of such maintenance, although perhaps only by a narrow margin, whereas portal vein blood flow alone is inadequate.

Although hepatic artery occlusion resulted in a liver *p*H considerably below normal, a further and more precipitous drop occurred when the portal vein was occluded 60 minutes after hepatic artery arrest. This gives a crude estimate of the extent to which the portal vein circulation contributes to liver maintenance. It should be emphasized that the hepatic artery remained clamped in these animals during portal vein occlusion.

Simultaneous occlusion of the hepatic artery and portal vein in the Eck fistula animals resulted in a rapidly falling *p*H to a mean of 6.43 after 1 hour. Following 60 minutes of circulatory arrest of the liver, the occluding clamps were removed. A striking change in *p*H followed, rising from a mean value of 6.43 to 6.71 in 5 minutes. Approximately 45 minutes elapsed after restoration of blood flow before the *p*H attained a normal level. Recovery time was somewhat slower than expected and probably represented circulatory impairment in the liver tissue. This delay in re-establishment of circulation was also reflected in a decreased rate of disappearance of radioactive sodium from the liver following various periods of hepatic afferent circulatory arrest. Crowell's hypothesis concerning the formation of miliary clots during circulatory stasis must be considered in the interpretation of these findings.

Hepatic anaerobic metabolism is associated with glycolysis and a rise in both lactates and pyruvates. It is probable that these products of anaerobic metabolisms are primarily responsible for the increasingly acid reactions as observed in the liver experiencing circulatory arrest.

CONCLUSIONS

1. The normal mean *p*H of the liver was found to be 7.06.

2. Occlusion of the portal vein alone for 1 hour resulted in a *p*H of 6.94.

3. Occlusion of the hepatic artery resulted in a mean depression of *p*H to 6.79 after 1 hour.

4. Occlusion of the portal vein for a period of 1 hour after the hepatic artery had been arrested for 1 hour resulted in a mean *p*H of 6.30.

5. Total afferent hepatic vascular occlusion of 1 hour's duration resulted in a *p*H drop to a mean of 6.43. This rose to 7.00 one hour following removal of the occluding clamps.

6. Hydrogen ion activity correlates well with various degrees of hepatic circulatory impairment.

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A COMPARISON OF THE HEMATOLOGIC RESPONSES FOLLOWING THE ROUTINE PRENATAL ADMINISTRATION OF INTRAMUSCULAR AND ORAL IRON

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AN APPRECIABLY lowered hemoglobin concentration is not uncommon in pregnant women. Quite often large volumes of blood are administered to these women in an attempt to correct such deficits. For instance, from July 1954 to July 1955, 31 per cent of the patients on the obstetric service at Parkland Memorial Hospital were given 1 or more pints of blood. It should be pointed out that practically all of the patients cared for at this institution are from an extremely low income group; most of them are negroes. Their diets not infrequently must be considered qualitatively grossly inadequate for pregnant women. The clinic load is large and dietary instruction by trained personnel is not always ideal. Patient co-operation not infrequently appears to be poor.

A systematic investigation of this major obstetric problem has been undertaken to determine the cause or causes of the high incidence of anemia in these patients. As a part of this investigation, studies have been carried out which attempt to answer two questions regarding the value of routine administration of iron during pregnancy: (1) Will the administration of iron alone result in significant hematologic improvement even though the diet is qualitatively poor? (2) Is the frequency of failure of self-administration of oral iron or, less likely, faulty absorption of sufficient magnitude to warrant the routine parenteral administration of iron during pregnancy?

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MATERIALS AND METHODS

Patients believed to be late in the second trimester of pregnancy on the basis of their stated last menstrual period were selected for this study at the time of their first visit to prenatal clinic and assigned at random to one of 3 groups prior to any other clinical or laboratory evaluation. One group was given a total of 1,000 milligrams of iron intramuscularly as iron-dextran. Five milliliters containing 250 milligrams of iron were injected deep into each buttock at the first visit and again 1 to 3 weeks later. Another group received tablets of ferrous gluconate 0.3 gram and were instructed to take 3 tablets a day throughout the remainder of pregnancy. The subjects in this group were urged repeatedly by the clinic physicians and secretary to take the medication. A third group was given tablets of lactose and instructed to take 3 each day.

Blood was drawn from an antecubital vein into mixed oxalate. The concentration of hemoglobin was measured in duplicate as oxyhemoglobin with a Beckman model B spectrophotometer. A search for red cell sickling after treating with sodium metabisulfite was carried out in each case, according to the method described by Ham. If sickling was noted, or in the absence of sickling if the hemoglobin level was less than 10.0 grams, the types of hemoglobin present were determined with a Spinco model R paper electrophoresis system. The hemoglobin patterns in all cases studied revealed either the combination of hemoglobin S (sickle hemoglobin) with hemoglobin A (normal adult hemoglobin) or normal adult

hemoglobin alone (A-A). The hemoglobin concentration was measured in duplicate again when each subject was admitted to the hospital for delivery. Only those patients who were noted to be bleeding at that time or were delivered less than 6 weeks after the start of therapy were excluded from this study.

Observations were made in 49 women who received iron intramuscularly, in 74 women who were given tablets of ferrous gluconate, and in 49 women who received only a placebo. The interval between the initial and final measurements in each group ranged from a minimum of 6 to a maximum of 20 weeks. The average intervals were 11 weeks, 12 weeks, and 11 weeks for the intramuscular iron, oral iron, and placebo groups respectively. All hemoglobin values are expressed as grams per 100 milliliters.

RESULTS

In the 49 subjects who were not given iron the initial mean hemoglobin level was 11.0 grams and varied from a low of 8.8 grams to a high of 12.8 grams while the final concentration averaged 11.3 grams and ranged from 8.8 to 13.7 grams. In the 49 subjects who received 1,000 milligrams of iron intramuscularly the initial mean hemoglobin level was 10.9 grams and ranged from 8.8 to 13.0 grams per 100 milliliters; the final concentration averaged 12.5 grams and ranged from 10.7 to 15.0 grams. In the 74 patients who were given tablets of ferrous gluconate the initial hemoglobin concentration averaged 11.1 grams and ranged from 8.2 to 13.9 grams while the final mean hemoglobin level was 12.5 grams and ranged from 10.3 to 14.5 grams. Therefore, the average increase in the concentration of hemoglobin in each group was 0.3 gram, 1.6 grams, and 1.4 grams respectively.

TABLE I.—INITIAL AND FINAL HEMOGLOBIN LEVELS IN PREGNANT SUBJECTS RECEIVING NO SUPPLEMENTAL IRON, IRON-DEXTRAN INTRAMUSCULARLY, OR FERROUS GLUCONATE ORALLY (EXPRESSED AS PER CENT OF EACH GROUP)

Hemoglobin	*Placebo*		*Intramuscular*		*Oral*	
gm./100 ml.	*Initial*	*Final*	*Initial*	*Final*	*Initial*	*Final*
<10 gm.	12	16	12	0	13	0
10 gm. or more	88	84	88	100	87	100
11 gm. or more	42	53	34	96	48	91
12 gm. or more	20	28	14	69	18	65
13 gm. or more	4	8	2	39	4	40

In Table I is presented a more detailed analysis of the patients in each group according to their hemoglobin concentrations at the beginning and end of the study. Fifty-seven per cent of the total of 172 patients had a hemoglobin concentration of less than 11.0 grams and 12 per cent of less than 10.0 grams at the time of their first clinic visit. At the end of the study no patient receiving oral or parenteral iron had a hemoglobin level below 10.0 grams compared to 16 per cent of those who received no supplemental iron. Furthermore, at the end of the study 96 per cent of the patients receiving intramuscular iron and 91 per cent of those given oral iron had a hemoglobin concentration of 11.0 grams or more whereas only 53 per cent of the subjects who received no iron achieved this level. Similarly, 69 per cent of those receiving intramuscular iron and 65 per cent of those given oral iron had a hemoglobin concen-

TABLE II.—CHANGES IN THE HEMOGLOBIN CONCENTRATION IN PATIENTS WITH AN INITIAL LEVEL OF LESS THAN 10.0 GRAMS PER MILLILITERS

	Placebo			*Intramuscular iron*			*Oral iron*		
	Initial, gm.	*Final, gm.*	*Interval, weeks*	*Initial, gm.*	*Final, gm.*	*Interval, weeks*	*Initial, gm.*	*Final, gm.*	*Interval, weeks*
1.....	8.8	9.3	11	8.8	11.9	7	8.1	12.2	16
2.....	9.5	11.1	8	9.0	12.3	7	8.1	13.0	10
3.....	9.7	9.7	10	9.4	11.3	8	9.0	10.3	19
4.....	9.8	8.8	15	9.6	12.3	13	9.0	11.9	12
5.....	9.8	9.7	16	9.9	11.0	7	9.0	13.0	11
6.....	9.8	10.6	10	9.9	13.5	11	9.3	12.2	6
7.....							9.3	13.4	7
8.....							9.6	10.8	18
9.....							9.9	12.2	7
Mean	9.6	9.9	12	9.4	12.1	9	9.1	12.1	12

tration of 12.0 grams or more when admitted, but only 28 per cent of those without iron supplementation were in this category.

As shown in Table II, considerable hematologic improvement was demonstrated by the time of admittance for delivery in the 15 patients with an initial hemoglobin concentration of less than 10.0 grams who received iron irrespective of the route of iron administration. The hemoglobin level in the 6 subjects who received iron intramuscularly rose from an average of 9.4 grams to 12.1 grams with none below 11.0 grams. In the 9 subjects who received oral iron the mean hemoglobin concentration increased from 9.1 grams to 12.1 grams and in all but 2 the final level was 11.0 grams or more. However in the 6 subjects with an initial hemoglobin level below 10.0 grams who received no iron, the mean concentration rose only from 9.6 grams to 9.9 grams and in 4 of the 6 the hemoglobin level was below 10.0 grams when they were admitted for delivery.

The final concentration of hemoglobin had decreased 1.0 gram or more in 9 out of 49 who received no supplemental iron, in 1 out of 74 given oral iron, and in none of 49 given iron-dextran intramuscularly.

DISCUSSION

The value of routine iron supplementation during pregnancy again has been demonstrated. Prior to undertaking this study the possibility was entertained that not infrequently an appreciable impairment in hemoglobin synthesis might be due to deficiencies other than iron and consequently iron supplementation alone might be of little value in this indigent group. This does not appear to be the case.

It was considered much more probable that a lack of iron was the usual cause of anemia and that failure of self-administration of iron or, less likely, faulty absorption of iron would be so common that significant anemia would be seen often even though patients were given iron to be taken orally.

Preliminary observations in this laboratory as well as the reports of Scott and others have indicated that iron as iron-dextran could be administered in appreciable amounts with no adverse reactions. Therefore, it seemed worth while to study a comparable group of patients who had been given intramuscularly the iron requirements of pregnancy. With this therapy nearly all of the iron would be trapped within the body and could be utilized upon demand. One-thousand milligrams of iron were considered enough to supply both the iron that is transferred to the fetus (an average of 375 milligrams) and that which must be incorporated into maternal hemoglobin if an appreciable fall in its concentration is to be prevented as the plasma volume increases.

No advantage from administering iron intramuscularly over simply giving it orally was demonstrated. The average concentration in both groups at the end of the study was 12.5 grams per 100 milliliters. No patient had a hemoglobin level below 10.0 grams and more than 90 per cent of the patients had a level of 11.0 grams or more when admitted for delivery.

These results are not interpreted as indicating that there is no place for the use of iron-dextran intramuscularly in pregnancy but only demonstrate that for routine supplementation during pregnancy iron administered intramuscularly usually offers no advantage over iron taken orally.

CONCLUSIONS

1. The routine administration of iron to indigent pregnant patients presumably receiving a poor diet results in appreciable hematologic improvement.

2. The degree of improvement is not significantly better when iron is given as iron-dextran in a dose of 1,000 milligrams intramuscularly rather than dispensed as tablets of ferrous gluconate to be taken orally.

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A STUDY OF 158 CASES OF ESOPHAGEAL VARICES

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MASSIVE BLEEDING from esophageal varices comprises about one-third of major upper gastrointestinal hemorrhages and results in about three-fourths of the deaths from this cause. The purpose of this study is to record our experience with 158 cases of esophageal varices seen at the Wadsworth Veterans Administration Hospital in the 3 year period, 1953 to 1955 inclusive. All cases were substantiated by x-ray, endoscopy, autopsy, or evidence that bleeding could be controlled by esophageal tamponade.

ETIOLOGY OF ESOPHAGEAL VARICES

It is well accepted today that the main etiologic factor in the development of esophageal varices is portal hypertension, caused by extrahepatic or intrahepatic portal bed block. The former usually results from portal vein thrombosis and generally occurs in children or young adults. It accounts for about 10 per cent of the cases of bleeding esophageal varices but, of course, is less than that in a Veterans Hospital.

Intrahepatic portal bed block is thought to be due to obstruction of hepatic venules by obliterative fibrosis and distortion of cellular architecture. The various forms of cirrhosis, especially Laennec's cirrhosis, account for the great majority of the cases of bleeding esophageal varices. In our series, Laennec's cirrhosis accounted for 132 or 83 per cent of the 158 cases of esophageal varices, and an even greater percentage of those that bled. Heavy alcoholic consumption was established in 92 per cent of these cases of Laennec's cirrhosis, and it is interesting to note that among these the average period of alcoholism before complications appeared was 17.3 years.

Since alcoholic cirrhosis caused by far the great majority of cases of bleeding varices in this hospital, our attention for the remainder of this study will be focused on the 132 cases of Laennec's cirrhosis. The incidence of the other etiologic types can be seen in Table I.

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SURVIVAL IN PATIENTS WITH CIRRHOSIS AND VARICES

Patients with cirrhosis of the liver can be roughly divided into two nearly equal groups: those who develop esophageal varices and die from hemorrhage and its complications, and those who do not develop esophageal varices and who usually expire as a result of spontaneous hepatic coma or intercurrent infection. Weinberg performed autopsies on 30 cirrhotic patients and found 57 per cent had varices. Palmer and Brick (16), in an endoscopic study of 47 patients with histologically proved portal cirrhosis, found 67 per cent with varices. Why only a little over half of the patients with cirrhosis develop esophageal varices is not completely understood. The number and size of development of alternate collateral channels probably play a part. The existence of congenital portacaval shunts in 4 out of 8 unselected fresh human cadavers examined by Madden and Lore is an interesting and significant observation.

Recent advances in medical dietary treatment have effectively reduced the number of deaths from intercurrent infections and have delayed death from spontaneous hepatic coma. But these advances have given little evidence of helping those patients with esophageal varices. The great majority of these patients bleed, and usually they die as a result of hemorrhage and its complications.

In Table II, the published survival statistics of patients with portal cirrhosis and

TABLE I.—ETIOLOGY OF 158 CASES OF ESOPHAGEAL VARICES

	No. of cases
Laennec's cirrhosis	132
Fatty infiltration of liver	1
Postnecrotic cirrhosis	6
Biliary cirrhosis	1
Portal vein thrombosis	4
Obliterative phlebosclerosis of hepatic veins in a case of Buerger's disease	1
Metastatic carcinoma of liver	3
Primary hepatoma with invasion of portal vein	1
Adenocarcinoma of gallbladder with obstruction of common bile duct	1
Hemochromatosis of liver	1
Heart failure with cardiac cirrhosis	3
Emphysema lung*	3
Lobar pneumonia*	1

*Palmer (17) noted the occurrence of esophageal varices in chronic pulmonary disease. While chronic pulmonary disease is not known to give rise to esophageal varices, yet he believed that the high incidence of esophagitis and the usual alterations of vascular dynamics in chronic pulmonary disease suggested association.

bleeding esophageal varices are given and compared with those for this hospital. In each of these large series over 50 per cent were dead within 1 year of the first hemorrhage.

STATISTICAL ANALYSIS OF CASES

In 132 cases of Laennec's cirrhosis with proved varices in our series, the breakdown statistics were as follows:

A. One hundred and eighteen or 89 per cent bled with the following results:
   1. One hundred and four or 88 per cent were dead within 1 year of the first hemorrhage.
   2. The average survival after the first hemorrhage was 6.4 months.
   3. The average number of hemorrhages per patient was 1.9.
   4. The average amount of blood given per hospital episode was 9 pints.
   5. Of those who bled and died:
      a. Twenty per cent died of exsanguination and shock.
      b. Fifty-nine per cent died of exogenous hepatic coma secondary to hemorrhage.
      c. Fourteen per cent died of a combination of shock and coma. We could not be sure which was the major factor.
      d. Seven per cent died of miscellaneous causes (pneumonia, complications of emergency surgery).
      e. The average age at death was 51.6 years (youngest 27 years).

B. Only 6 per cent (8 of 132) died of spontaneous coma without bleeding.

C. Five per cent (6 of 132) had virgin varices (no bleeding while under observation).

D. Sixty-one per cent (80 of 132) of these cirrhotic patients were dead within 1 year after the first signs and symptoms of cirrhosis were noted by themselves or their physicians.

E. The average survival after the first signs and symptoms of cirrhosis were noted was 17.8 months.

F. Autopsies were performed on 105 of the patients expiring, and there was evidence of esophagitis, esophageal ulcers, or mucosal ulcerations in 50 per cent of these.

G. The percentages of miscellaneous diseases found at autopsy in these 105 patients with Laennec's cirrhosis were:
   1. Gallbladder disease, 12.6
   2. Gallstones, 10
   3. Pancreatitis, 8
   4. Pyelonephritis, 8
   5. Pneumonia, 12.6
   6. Emphysema, 2.5
   7. Diaphragmatic hernia, 5
   8. Gastroduodenal ulcer, 11

H. Frequency of physical signs reported in the 132 cases of Laennec's cirrhosis, expressed in percentages was:
   1. Liver enlargement, 75.0
   2. Spleen palpably enlarged, 19.0
   3. Jaundice present, 69.0
   4. Ascites, 71.0
   5. Spider angiomas, 59.0
   6. Dilated abdominal veins, 19.0
   7. Pectoral alopecia, 7.0
   8. Palmar erythema, 10.6
   9. Testicular atrophy, 19.0
   10. Gynecomastia, 3.0
   11. Dependent edema, 29.0
   12. Ecchymoses of skin, 1.5
   13. Signs of vitamin deficiency, 12.0
   14. Hemorrhoids, 10.0

MANAGEMENT OF PATIENTS WITH BLEEDING

Because of the toxic effects of blood absorbed from the gastrointestinal tract in cirrhotic patients, it is most important to stop bleeding in these patients as soon as possible. This is as important as replacing the blood that has been lost. Prevention of exogenous hepatic coma secondary to bleeding is more effective than attempts at detoxification therapy after coma ensues. Attempts to remove blood already pooled in the gastrointestinal tract by gastric lavage, laxatives, and enemas should be tried. Neomycin should be given per Sengstaken tube to depress intestinal flora and thus

slow down the breakdown of proteins to form ammonia. Blakemore found that if balloon tamponade was inserted immediately without delay, the recovery rate was 50 per cent higher. It is an important therapeutic as well as diagnostic step. Many investigators have established the role of absorbed nitrogenous products from the gastrointestinal tract in producing high blood ammonia levels and central system symptoms. There are undoubtedly other noxious agents in addition to ammonia, for exogenous coma resulting from hemorrhage in these patients with diseased livers is a much more serious disease than coma resulting from ingestion of ammonia salts by these same patients.

Balloon tamponade was used in 49 per cent of our cases and bleeding stopped in 75 per cent of these patients. In 43 per cent of these cases the bleeding recurred on removal of the tamponade. So, while the balloon tamponade is an effective emergency measure, it is only a temporary one in at least half of the cases. Because of this high rate of recurrent bleeding, Linton (10, 12) has advocated emergency transthoracic transesophageal ligation of varices and reports on a series of 20 cases with only a 10 per cent mortality. The low mortality indicates, I think, that he has been extremely careful in selecting his cases. This operation is only a temporary procedure itself, and definitive shunts must be performed within a few months or these patients run the hazards of rebleeding. Welch (24) introduced the transabdominal route for ligation of varices, this route having the advantage of being more familiar to the general surgeon and allowing him the opportunity to deal with gastroduodenal ulcers which may be the source of bleeding in from 10 to 16 per cent of bleeding cirrhotic patients. In our patients, 11 per cent had gastroduodenal ulcers as a source of the bleeding.

If liver function tests indicate adequate liver function to warrant surgical intervention, and if emergency ligation of esophageal varices is contemplated, it should be done as soon as replacement therapy has been completed, for procrastination and repeated short trials of tamponade with rebleeding only lead to further deterioration of the patient. Our own experience with emergency ligation of bleeding varices proves this point, and the results have been very discouraging. Of the 7 patients operated on, only 1 survived. That patient later had a portacaval shunt and is well today. I believe that procrastination was at least partially responsible for these poor results, for liver function tests were fairly good in at least half these patients at the start.

TABLE II.—COMPARISON OF SURVIVAL STATISTICS FOR CIRRHOSIS WITH BLEEDING VARICES

Investigators	*Per cent dead within 1 year after the first hemorrhage*
Ratnoff and Patek (18, 20)	70
Shull (3)	63
Douglas and Snell	50
Reynell	80
Nachlas	72
Welch (25)	80
Wadsworth Veterans Hospital (Los Angeles)	88*

*104 of 118.

Three of the deaths were from hepatic coma; 1 patient died from peritonitis 10 days postoperatively because of leakage of the gastrotomy wound; 1 died 9 days postoperatively from right ventricular heart failure secondary to massive atelectasis of the left lower lobe of the lung; and the final death was from exsanguination and shock on the operating table in a patient with a shunt failure and rebleeding. These cases are summarized in Table III.

There are many surgeons who believe that operations, as already described, which have to be followed by a second major operation within a few months are too heavy a burden for the cirrhotic patient. O'Sullivan and Child (6) have suggested that emergency portal decompression, if the hepatic reserve is at all reasonable, may be preferable. O'Sullivan reported on a series of 9 patients so treated with a 33 per cent mortality. Child suggested that emergency portacaval shunt performed under hypothermia might give better results. Body

TABLE III.—PATIENTS WITH LAENNEC'S CIRRHOSIS WHO HAD EMERGENCY LIGATION OF BLEEDING ESOPHAGEAL VARICES

Patients Age, yrs.	*TT or TA*	*Rebled*	*Expired*	*Survived*	*Came to shunt*	*SA*	*SB*	*CF*	*Proth., per cent*	*BSP, per cent*	*TT*
LAD 60	TT	Yes	In coma 5 days postoperatively			4.5	0.86	1+ 2+	100	19.9	4.4
SL 36	TA		In coma 2 days postoperatively			4.3	1.8		100		5.8
FB 45	TT			Yes	Yes						
EMP 65	TA		Right ventricular heart failure secondary to massive atelectasis L.L.L. lung 9 days P.O.			2.3	1.9	4+	100	39.4	4.4
HLK 54	TA		Peritonitis secondary to leakage gastrotomy wound 10 days P.O.								
PEM	TT		In coma 1 day P.O.			2.5		2+ 4+	88		8.6
LGB	TA		On operating table in shock								

TT—Transthoracic
TA—Transabdominal
SA—Serum albumin
SB—Serum bilirubin
CF—Cephalin flocculation
Proth.—Prothrombin
TT—Thymol turbidity
BSP—Bromsulphalein

TABLE IV.—SURGICAL MORTALITY AND SHUNT FAILURE STATISTICS FOR INTRAHEPATIC GROUP

Surgeon	*No. of cases*	*Type of shunt*	*Year reported*	*Per cent failures*	*Operative and P.O. mortality, per cent*
Blakemore.....	203	Usually portacaval end-to-side	1955	15	Over-all—19 Good risk cases—9.4 Poor risk cases—39.6
Linton (9).....	104	Two-thirds were splenorenal	1956	17	Over-all—15
Child (6).....	56	Portacaval end-to-side	1956	None	Over-all—14
Jahnke (11).....	30	Usually portacaval end-to-side (2 were extrahepatic)	1956	6.6	Over-all—6.6

temperatures of 26 to 28 degrees C. necessitate less anesthesia and decrease hepatic metabolic demands. Bernhard, McMurrey, and Curtis have shown through animal experimentation that hypothermia effectively protects the liver, even when there is afferent vascular occlusion up to 1 hour. Histologic and liver function tests were normal afterward. In normothermic animals, this procedure resulted in 100 per cent mortality. We have had no experience in emergency shunts.

In the majority of patients, liver reserve is not good enough for these extensive surgical procedures. In these patients, Blakemore's method of prolonged tamponade appears to be worthy of trial while attempting to restore liver compensation in preparation for a possible shunt procedure later.

After 72 hours, the balloon is deflated but left *in situ* on suction to check for rebleeding. If rebleeding occurs, the balloon is immediately reinflated and left in place for from 1 to 2 weeks or longer as may be necessary

in an attempt to prepare the patient for surgery. During this time liver compensation is restored, if possible, by tube feedings, parenteral vitamins, blood, and plasma. Blakemore does not mention what complications occur in his cases in the way of esophagitis, tracheitis, aspiration pneumonia, or rupture of the esophagus from prolonged tamponade. Certainly a reasonable risk could be accepted in the light of the high mortality from rebleeding.

DEFINITIVE SURGICAL MANAGEMENT OF INTRAHEPATIC GROUP

The portal-systemic vein shunt operations are generally accepted as the most effective method of lowering portal hypertension, decompressing the liver, and preventing future hemorrhages. However, other operations still have their advocates and their place. Total gastrectomy has been advocated by Wangensteen and Baronofsky for both intrahepatic and extrahepatic hypertension, with the thought that the acid peptic reflux is the etiologic factor in the large proportion of bleeding varices. However, this operation is difficult and tedious because of extensive collaterals, and the removal of the stomach puts a serious handicap on patients who are already poorly nourished because of a sick liver. Esophagogastric resection is advocated by Shumacker and King, Cooley and DeBakey, and others. In those cases in which bleeding recurs because of shunt failures, this operation may become a necessity. In Table IV is a summary of the statistics on surgical mortality and shunt failures as found in the literature.

In the series reviewed at this hospital, 7 portacaval and 2 splenorenal shunts were done during the period under study or the patients were readmitted for some surgical complication from shunts done at an earlier date. These cases are summarized in Table V. There was 1 shunt failure in a portacaval end-to-side shunt. The operation was performed under considerable difficulty because of marked inflammatory reaction about the portal vein. The patient rebled, was taken back to surgery for transesophageal ligation of the varices, and died on the table. This case accounted for the only operative and postoperative death and the only shunt failure, an incidence of 11 per cent.

TABLE V.—STATISTICS ON 9 PATIENTS WITH LIVER CIRRHOSIS WHO HAD SHUNT OPERATIONS

Patient Age, yrs.	*Type shunt*	*Living or expired*	*Comments*
LRP 59	PC ES	Living 7½ yrs.	Rebled from gastric ulcer 4 yrs. P.O., requiring subtotal gastrectomy
FEB 45	PC ES	Living 1½ yrs.	Feeling fine
RSW 39	PC ES	Living 4 yrs.	Feeling fine
OWB 56	SR	Living 6 yrs.	Rebled gastric ulcer 1 year P.O., requiring wedge gastrectomy
SLK 50	PC ES	Expired 4½ yrs.	Developed ammonia intoxication from high protein diet
CRW 55	PC ES	Expired 1 yr. P.O.	Hemorrhage from duodenum ulcer complicated by pneumonia
VS 60	SR	Expired 5 yrs.	Right hemicolectomy for adenocarcinoma. Leaked from anastomosis
LGB 41	PC ES	Expired few days postshunt	Rebled from varices P.O. Expired in shock during transthoracic ligation of varices
FFP 41	PC ES	Living 1 year	Feeling fine

PC—Portacaval ES—End-to-side SR—Splenorenal

The follow-up in our series was as follows: (1) Five patients are still living and in good health without ascities. (2) The rest have expired for the following reasons: (a) ammonia intoxication 4½ years postoperatively; (b) hemorrhage from a duodenal ulcer 1 year postoperatively; (c) peritonitis following a right hemicolectomy for adenocarcinoma 5 years postoperatively; (d) shock during transthoracic ligation of varices. The incidence of postoperative gastroduodenal ulcers was 33 per cent, and in 22 per cent of these cases hemorrhage occurred requiring subtotal gastrectomy or wedge gastrectomy. These patients are doing fine.

DISCUSSION OF THE SHUNT OPERATIONS

While portacaval end-to-side vein anastomosis is technically the easiest and provides the best decompression with less chance

TABLE VI.—COMPARISON OF ABNORMAL LIVER FUNCTION TESTS IN 2 GROUPS

Laboratory tests	*Called abnormal if:*	*Abnormal group A, per cent*	*Abnormal group B, per cent*
Serum albumin	Below 3 grams	44	8
Bromsulphalein	Over 20% 45/min.	72	3
Cephalin flocculation	More than 2+	64	8
Prothrombin	Less than 40%	4	0
Thymol turbidity	Over 10 units	40	8
Thymol flocculation	More than 1+	41	0
Alkaline phosphatase	Over 10 units	25	17
Total cholesterol	Less than 150 mgm. %	31	50
Cholesterol esters	Less than 65%	45	0
Serum bilirubin	More than 1.5 mgm. %	92	37
Icterus index	More than 10 units	90	29

Group A, Total series of 132 patients with cirrhosis.
Group B, Patients with cirrhosis surviving surgery or hemorrhage.

of failure from thrombosis, there is still a question in the minds of many surgeons as to the effect of diverting the entire portal blood flow from the liver. Whipple demonstrated that the Eck fistula dog was under a distinct handicap in its ability to fabricate certain essential proteins. Large and associates (19) have recently shown that animals with Eck fistulas can withstand only small amounts of carbon tetrachloride poisoning, while dogs with side-to-side portacaval shunts can tolerate almost as much carbon tetrachloride as normal dogs. Over half of Blakemore's patients, who died after portacaval end-to-side shunts, died of liver failure. Linton noted double the number of liver failures among the portacaval shunts as compared to the splenorenal shunts. The portacaval end-to-side procedure presents the danger of ammonia intoxication to a greater degree also. Child (4) reported 8 instances of coma and 5 deaths, Jahnke (11), 3 deaths, and there was 1 death in our series from ammonia intoxication. The incidence of ammonia intoxication is much less in the side-to-side portacaval and splenorenal shunts.

TABLE VII.—LIVER FUNCTION TESTS BEFORE SHUNT SURGERY AND IN LONG TERM FOLLOW-UP AS PUBLISHED BY LINTON

Status of patients liver function tests	*Serum albumin, per cent*	*Cephalin flocculation, per cent*	*Serum bilirubin, per cent*	*BSP, per cent*
Improved.....	29	40	30	23
Unchanged....	53	40	50	31
Worse.....	18	20	20	46

It would seem, therefore, that despite the popularity and excellence of the portacaval end-to-side shunt, we should perhaps have some reservations to its routine use in all cases. The side-to-side portacaval shunt when technically possible and the splenorenal shunt when the splenic vein is good sized may be safer despite the greater tendency to thrombosis and hemorrhage.

FOLLOW-UP TREATMENT AFTER SHUNT OPERATIONS

It is most important that these patients be given careful follow-up treatment. The gravest problem the surgeon faces in this phase of the treatment is that of chronic alcoholism. The reason alcoholic cirrhosis holds such a bad prognosis as compared with biliary and posthepatitic cirrhosis is that the alcoholic, in addition to having a sick liver is a social-psychiatric problem as well. If he continues to drink, his disease continues to progress, and he will die of his cirrhosis. In checking total mortality statistics on his cases, Linton (9) found that shunts performed for the various types of cirrhosis gave these figures: 50 per cent in alcoholic cirrhosis, 32 per cent in postnecrotic cirrhosis, and 25 per cent in biliary cirrhosis. Success in overcoming this problem demands co-operation and patience on the part of the patient, doctor, and family. To gain freedom from abnormal dependence on alcohol, an alcoholic must abstain from the use of alcohol absolutely and permanently. Social education and group psychotherapy as offered by Alcoholics Anonymous can be of great aid. Psychiatric help may be needed.

In addition to the discontinuance of alcohol, attention should be given to the patient's diet. This should contain adequate vitamins and caloric content, but be low in fats and moderate in proteins. Also, these patients should be alerted to and protected from the possibility of gastroduodenal ulcers. Patients with cirrhosis have an increased incidence of these ulcers, and hemorrhage from a gastroduodenal ulcer is just as dangerous as from esophageal varices. Regular 6 month liver

TABLE VIII.—COMPARISON OF LIVER FUNCTION TESTS TAKEN PREOPERATIVELY AND POSTOPERATIVELY FROM 1 TO 7 YEARS AFTER PORTAL-SYSTEMIC SHUNT OPERATIONS

Patient Age, yrs.	*Type shunt*	*Before After*	*S.A.*	*S.B.*	*C.F.*	*Proth., per cent*	*T.T.*	*BSP, per cent*
LRP 59	Portacaval end-to-side	Before	4.0	N.	3+	85	13.0	
		After	4.3	N.	1+, 3+	100	3.5	1
FEB 45	Portacaval end-to-side	Before	4.0	N.	1+	100	9.0	14.5
		After	4.2	N.	0	100	6.2	12.6
RSW 39	Portacaval end-to-side	Before	3.8	2.1	0	100	5.3	23.0
		After	4.7	0.98	1+	100	7.2	
OWB 56	Splenorenal shunt	Before	4.7		0	88		1.8
		After	4.7	N.	1+	100	7.25	5.6
SLK 50	Portacaval end-to-side	Before	3.2	0.54	2+, 2+	88	9.0	
		After	2.6	4.48	2+, 3+	48	26.5	
CRW 55	Portacaval end-to-side	Before	5.2		1+, 3+	100	8.1	25.4
		After	4.3	0.45		100	5.0	13.8
VS 60	Splenorenal shunt	Before						
		After	3.3	N.	0, 1+	77	7.7	
FFP 54	Portacaval end-to-side	Before	4.2	0.74	4+, 4+	100	5.8	16.5
		After	4.1	3.38	1+, 2+	88	5.8	38.3

SA—Serum albumin
SB—Serum bilirubin
CF—Cephalin flocculation
Proth.—Prothrombin
TT—Thymol turbidity
BSP—Bromsulphalein

function tests help to keep regular contact with the patient and check his prognosis.

WILL THE SHUNT OPERATION PROLONG THE LIFE OF THE CIRRHOTIC PATIENT?

There has been no adequate comparable follow-up of cirrhotic patients treated medically to answer this question conclusively. As has been pointed out by Nachlas and Child (5), the 50 to 80 per cent mortality figures following hemorrhage, usually cited by surgeons to prove the effectiveness of their shunt operation and follow-up statistics, are not altogether valid. These published mortality statistics include many patients in advanced stages of cirrhosis and many terminal when hemorrhage occurs. In patients with very advanced liver disease, surgery can offer no more than a medical regimen. Reference to Table VI quickly reveals the marked difference in the percentage of abnormal liver function tests in our 132 patients with Laennec cirrhosis and the percentage of abnormal tests in those patients who survived hemorrhage or major surgery. Survival after a major operation or major hemorrhage indicates fairly good liver function.

What is needed is a carefully followed group of medically treated cirrhotic patients with the comparable degree of liver reserve that is required in our criteria for performing the shunt operations. When such a group of patients has been treated by a strict medical diet regimen—including elimination of alcohol—followed up, and statistically analyzed, then better evaluation of the effectiveness of the shunt operations can be made.

Likewise, there is no reason to believe that portal decompression improves liver function or impairs liver function to any significant degree. The possible exception to this statement might be the questionable deleterious effects of the complete shunting of portal blood away from the liver as in the end-to-side portacaval shunt discussed earlier. Blakemore and Linton (9, 10) both with 10 year follow-ups on large series of surgical portal-systemic shunts, are impressed with the dramatic improvement of their patients postoperatively as to general well being, strength, and appearance. This point is shown in Table VII by a comparison of liver function tests before surgery and in careful follow-ups in Linton's series.

Analysis of the liver function tests in our patients undergoing portal systemic shunt surgery confirms Linton's findings. In Table VIII preoperative and follow-up liver function tests on 8 patients who successfully underwent shunt surgery are compared.

In conclusion, it can be stated with certainty that the portal-systemic shunts have proved their ability to protect the patient from the hazards of future hemorrhages, and in this way do prolong his life. However, the basic liver damage remains. The years of life remaining to the patient depend on the degree of liver damage and the strictness with which he adheres to the postoperative medical dietary regimen.

SUMMARY

Massive bleeding from esophageal varices comprises about one-third of the major upper gastrointestinal hemorrhages and results in three-fourths of the deaths from this source. In this study we have presented 158 cases of esophageal varices seen at the Wadsworth Veterans Administration Hospital from 1953 to 1955 inclusive. In 132 of these cases, Laennec's cirrhosis was the etiology of portal tension and esophageal varices. A detailed statistical analysis of these cases is given.

In cirrhotic patients, the portal-systemic vein shunts have proved their ability to prevent future hemorrhages. These operations can be performed with a reasonable mortality of from 10 to 15 per cent when the patients are properly prepared and selected. The basic liver damage remains, however, and the prognosis for future life depends on the extent of this liver damage and the strictness with which the patient adheres to the prescribed medical dietary regimen postoperatively.

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SURGICAL COMPLICATIONS OF VAGINAL HYSTERECTOMY

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THE POPULARIZATION of vaginal hysterectomy during recent years has led to its wider use by all physicians doing pelvic surgery. Actually, the indications for this operation have gradually become very general indeed. True, the experienced gynecologist finds this procedure not too difficult in the average, properly selected case. If ill chosen, however, even the specialist will have difficulty. As it is, the occasional operator is attempting hysterectomy now from below in the belief that the hazards are few and unimportant. As a result of this theory, preventable serious complications are occurring all too frequently.

In an effort to determine which surgical problems are the most common, the most serious, and how they can be avoided, 1,000 consecutive vaginal hysterectomies performed at the Emanuel Hospital, Portland, between December 15, 1949 and December 31, 1956, have been analyzed with special reference to the technical difficulties and the complications noted during surgery and the first 12 hours postoperatively. Embolus, infection, and other complications of the late postoperative period will not be considered at this time. The great majority of the patients were private. The operators were individuals with gynecologic privileges on this selected but otherwise open staff service, or were residents under supervision. The Heany technique was usually employed.

The problems were found to fall into the following categories: (1) difficult peritoneal entry; (2) injury to the bladder; (3) inability to deliver or remove the uterus; and (4) hemorrhage, immediate or delayed.

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Understandably, one difficulty often leads to another. For example, faulty entry into the anterior cul-de-sac was followed by laceration of the bladder in 4 instances. Previous surgery was responsible for scarring and advancement or fixation of the bladder in 2 of these cases. The visceral peritoneum of the uterus was mistaken for the parietal surface by carrying the dissection too deeply in another instance. Of course, this led to additional bleeding and confusion.

Lack of descensus with a narrow vagina and poor exposure were causal in 3 of the bladder lacerations in this series (Fig. 1). The occurrence of hypertrophic elongation of the cervix was also confounding to the operator in 1 case, a patient who sustained a perforation of the bladder. The surgeon exposed more and more of the cervix without reaching the peritoneal reflection promptly, and the bladder was then inadvertently entered. Happily, all of these lacerations healed per primam although a serious cellulitis complicated 1 case.

There were no direct injuries to the ureters in this series. This was fortunate because crushing, ligation, and severance of the ureter have been described in vaginal hysterectomy (Fig. 2).

More than one-third of the patients had had prior serious abdominal or vaginal surgery, inasmuch as 458 previous major procedures were recorded, and about half of these were abdominal. Certain of these led to more problems than others. Hysteropexy was the most serious. The majority of the 57 previous uterine suspensions, many of which were actually ventrofixations, and the 4 interpositions of the uterus with advancement of the bladder made for extremely onerous vaginal surgery (Fig. 3). In these latter

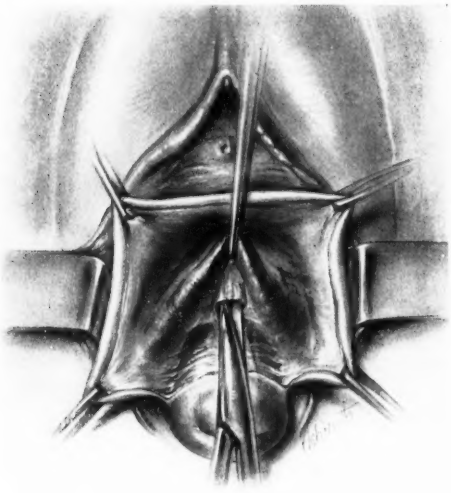

FIG. 1. Failure to delineate bladder wall from peritoneal fold allows perforation or laceration of bladder.

cases, it was very difficult indeed to open the anterior cul-de-sac. Nevertheless, despite these obstacles, vaginal hysterectomy was accomplished without catastrophe.

Previous surgery posed the vexing problem of separation of bowel in 10 cases in which dense small intestine adherence to the uterus was met (Fig. 4). Moreover, there were 44 patients who presented notable firm adhesions involving the uterus, and adnexa as well. Most of these, too, required a minor surgical struggle.

Many of the 22 cases of pelvic endometriosis diagnosed during vaginal hysterectomy could have been suspected also, and certain of these avoided by a more detailed history and careful examination under anesthesia. Save for several large ovarian endometriomas densely bound down, endometriosis did not actually constitute a serious problem, however, in spite of our concern for this problem.

The posterior cul-de-sac entry (Fig. 5) was rarely complicated and, fortunately, no injuries to the bowel occurred. Most of the patients had a redundant pouch of Douglas making this step easier, if anything. There were 180 enteroceles described and these were repaired, of course, as a part of the procedure which followed hysterectomy (Fig. 6).

Inability to deliver the uterus because of its large size or irregular shape required excision of myomas (Fig. 7) or morcellation of the uterus in a relatively few patients. The enucleation of such tumors was accomplished in 29 cases. Considerable ingenuity was obviously necessary in certain instances, and the removal of a fibroid of 5 centimeters in diameter or larger was effected in 8 patients. The largest tumor thus eliminated was 7.5 centimeters in diameter. Morcellation of the uterus was accomplished 4 times (Fig. 8). In 1 patient, the sizable corpus was removed in 3 pieces through the posterior cul-de-sac. In another, the entire uterus was split after the removal of a large fibroid, with individual delivery and excision of each half. Again, no complications resulted from these rather difficult maneuvers. Adenomyosis was re-

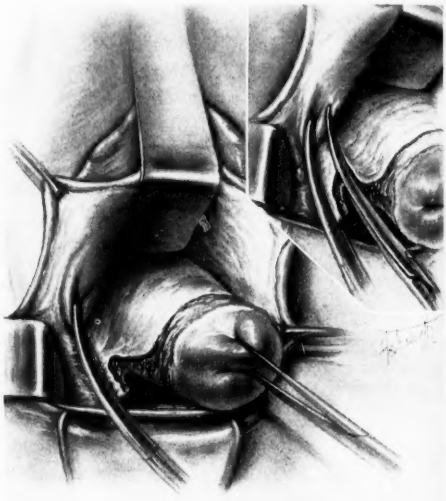

FIG. 2. Ureteral damage possible when clamps are applied too far laterally or when bladder dissection is incomplete.

ported in 173 patients. Enucleation of adenomyomas is impossible, of course, because of the absence of a pseudocapsule common to myomas. Hence, fragmentation is occasionally necessary.

Blood loss during surgery is admittedly most difficult to estimate. Be this as it may, 318 of the 1,000 patients required at least 1 transfusion for immediate blood replacement in surgery. This number does not include transfusions given in initial preparation, or for anemia later, but does embrace patients requiring anterior and posterior repair. The causal factors involved in blood loss were considered to be: (1) lack of adequate exposure; (2) faulty or incomplete ligation of vessels; (3) distortion or gross enlargement of the uterus; (4) varicosities and pelvic congestion; (5) excessive traction on the uterus; and (6) the inclusion of additional pelvic surgery.

Where poor visualization applied, the operator was unable to control multiple small or even larger individual bleeding points. The unfortunate extension of the dissection laterally, either beneath the symphysis or in the vicinity of the hemorrhoidal vessels, was almost universally fraught with danger from brisk bleeding. One patient required 15 transfusions and a secondary laparotomy 6 hours after hysterectomy because of unrecognized, uncontrolled bleeding from the subvesical plexus. Vaginal varices were also associated with poorly controlled bleeding in 3 women. Four patients were not known to be pregnant at the time of surgery and excessive ooze complicated these operations also.

FIG. 3. Ventrosuspension, cervical hypertrophy, and interposition of uterus complicate vaginal hysterectomy.

FIG. 4. Adherence of bowel to uterus and adnexa make vaginal hysterectomy difficult and dangerous.

The early recognition of massive intraperitoneal bleeding (Fig. 9) was established postoperatively in 4 other patients. Two of these were promptly reoperated upon abdominally as emergency cases. One had had a gross arterial hemorrhage from the incomplete ligature of the ovarian pedicle. Another patient bled from a poorly secured tube.

In addition to faulty ligation, undue traction on the uterus (Fig. 10) probably caused

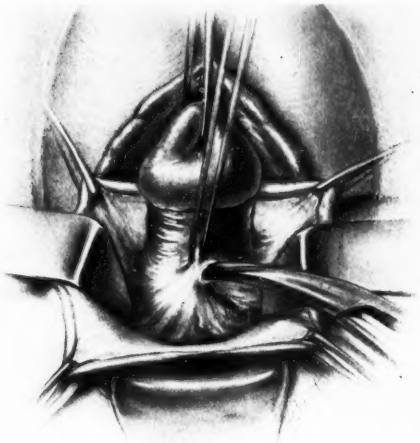

FIG. 5. Posterior cul-de-sac entry may damage bowel if high rectocele is present.

or contributed to hematoma formation in an indefinite number of patients. At least 10 patients with a postsurgical pelvic mass, sudden unexpected reduction in the blood count, or sanguineous vaginal drainage undoubtedly also sustained a concealed hemorrhage at operation. When proof was lacking, however, such cases have not been included in our data.

Persistent bleeding from the vaginal cuff resulting in shock occurred in 3 patients. The vagina of 1 was packed and another of the women was returned to the operating room for exploratory vaginal surgery. A small, free-spurting artery at the apex of the vagina was finally secured for control of the bleeding.

Out of 1,000 patients, but 112 underwent a vaginal hysterectomy only. In addition to the removal of the uterus by vaginal hysterectomy, the following operative procedures were also accomplished from below: anterior and posterior colporrhaphy in 764 cases; posterior colporrhaphy in 124; anterior colporrhaphy in 63; unilateral oophorectomy in 12; unilateral salpingectomy in 8; appendectomy in 6; bilateral oophorectomy in 2; and bilateral salpingectomy in 2.

In only 2 cases out of 30, can we blame the surgeon for ineptly doing a secondary intrapelvic procedure. In 1 of these, with the removal of an intact 7 to 8 centimeter cystoma, the pedicle was temporarily lost and brief, but alarming, bleeding was the result. The artery was fortunately ligated without having to resort to laparotomy.

Another patient was subjected to vaginal hysterectomy and a unilateral salpingo-oophorectomy. We learned later that the ovary was only minimally enlarged by what was then reported to be an innocent corpus luteum cyst. Deepening shock required exploratory abdominal surgery 8 hours postoperatively. Gross free blood in the peritoneal cavity was discovered. The infundibulopelvic vessels were found to be poorly tied and were resutured on one side. The patient required 10 transfusions, had a complicated, febrile course, but survived. There were no deaths in this series due to early, or late, complications.

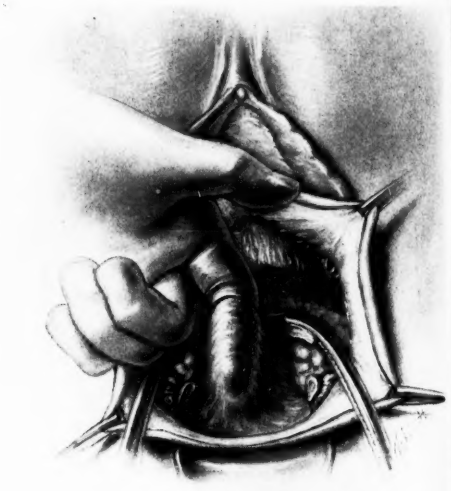

FIG. 6. Posterior cul-de-sac pouch requires excision to prevent vaginal hernia.

Blood loss in vaginal hysterectomy is directly proportional to the operating time —*if* the hemogram, occurrence of shock, need for blood replacement, as well as the estimate of blood lost are acceptable criteria. Measured blood loss is usually not possible in a retrospective study. Nevertheless, it was apparent to us that the skillful, expeditious surgeon did spill *less* blood than his slower, less accomplished colleague. To many, this observation is almost as significant as the immediate cause of hemorrhage.

True comparisons are rarely possible, of course. This would apply to the matter of blood loss in abdominal versus that in vaginal hysterectomy. Certainly, the more complicated gynecologic problems are usually approached abdominally. Yet, at this hospital, the vaginal approach is popular, as the statistics indicate. During the same 7 year period, 2,554 total abdominal and 1,000 total vaginal hysterectomies were accomplished at the Emanuel Hospital. In 53 per cent of the former and 41 per cent of the latter, transfusions were given after all indications were considered. This observation supports the often repeated statement that abdominal hysterectomy patients lose more blood than those operated upon vaginally—although not with true statistical significance.

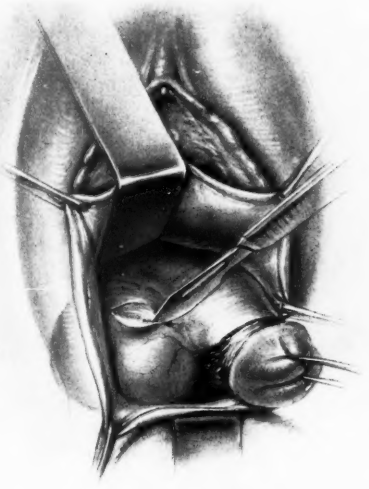

FIG. 7. Enucleation of myoma. Incision through pseudocapsule should be perpendicular to cervical axis to avoid major uterine vessels.

FIG. 8. Splitting or morcellation of uterus combined with enucleation of myomas facilitates delivery and removal of uterus.

A closer inspection of the case for vaginal hysterectomy, however, discloses that, of the 112 patients who sustained *only* the removal of the uterus from below, but 7 required a transfusion. Only 3 of these sustained an acute blood loss at surgery. Most blood is lost, we believe, during secondary procedures, particularly colpoperineorrhaphy.

DISCUSSION

It is apparent that there is no widespread agreement regarding the indications for vaginal hysterectomy. While most authorities hold that symptomatic prolapse is the problem most ideally corrected by this operation, other clinicians have extended the reasons for such surgery to merely "a uterus." A reasonable approach quite obviously lies somewhere between these poles.

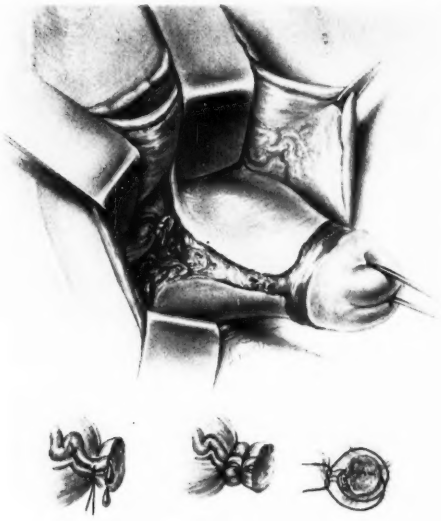

FIG. 9. Faulty ligation of vessels result in postoperative hemorrhage and hematoma formation. Lower figures: left, Major vessel pierced by suture but not secured; still bleeding. Middle and right, Doubly transfixed pedicle insures hemostasis.

Gray gives as indications for vaginal hysterectomy: (1) postmenopausal third degree prolapse of uterus with cystocele, rectocele, or enterocele; (2) premenopausal or postmenopausal second degree prolapse of uterus with cystocele, rectocele, or enterocele or with "combined syndrome" (multiple findings associated with uterus); and (3) menopausal uterine disease alone, either recurrent menometrorrhagia, or marked chronic cervicitis and cervical stenosis, "combined syndrome."

With regard to contraindications, the same lack of general acceptance prevails. Payne and also Rutherford, among others, often avoid vaginal hysterectomy in patients who have sustained major surgery, for example. On the other hand, Leventhal and Lazarus have stated that previous pelvic surgery does not constitute a contraindication to vaginal hysterectomy. TeLinde is less rigid, preferring to individualize. We favor the latter approach.

Contraindications to vaginal hysterectomy are, according to Gray: (1) malignancy of cervix or uterus (usually); (2) gross enlargement of uterus; (3) pelvic inflammatory disease, endometriosis; (4) ovarian tumors; (5) fixation of ligaments, lack of mobility; (6) previous abdominal surgery; (7) pseudodescensus with long cervix; (8) narrow vagina; (9) possible other intra-abdominal diseases; and (10) lack of experience, confidence, or enthusiasm of surgeon.

Our observations closely parallel those of Ingram, Withers, and Wright who reported their personal experience involving 308 vaginal hysterectomies. They purposely chose patients who had had previous major abdominal surgery in an effort to determine how difficult the removal of the uterus would be from below. They found that endometriosis and pelvic inflammatory disease posed the most serious problems (contraindications), but even uterine suspension did not prevent vaginal hysterectomy. Only 3 of their patients required a laparotomy because of complications or failure of surgery from below.

Even the most inquisitive and meticulous physician disregards essential details now and then. Or, he may minimize findings in the belief that his skill and experience will see him through the proposed surgery, despite his reservations. Nevertheless, more attention to the history and the physical findings, particularly when previous surgery, infection, mass formation, or periodic pain are reported, will avoid operative embarrassment and certain serious preventable complications. A careful examination under anesthesia should be a prelude to any major pelvic procedure whether vaginal or abdominal, yet this is often omitted, curiously enough, in the conservation of time.

Some operators prefer always to enter the posterior cul-de-sac first. Certainly, if the anterior cul-de-sac cannot be easily entered, a posterior approach is usually possible with delivery of the fundus, whereupon the anterior dissection can be completed over the finger as a guide. Widening of the anterior

peritoneal defect with the fingers will carry the ureters laterally. If one is certain to apply clamps close to the uterus all the way upward, the bladder and ureters will be further protected, sturdier pedicles and better vault support will be insured, and improved splinting of the tied vessels will be obtained. It may even be that avoidance of actual delivery of the fundus will eliminate tension on the parametria and limit the hazard of hemorrhage.

Unless a rare anterior enterocele is met, and assuming no previous bladder surgery, the anterior reflection of the parietal peritoneum will ordinarily be in line with the uterine arteries which can be used as guides. Extended search for the point of anterior entry should be delayed until the uterine vessels are ligated and severed. This method is especially helpful when the cervix is hypertrophic. Some prefer to avoid anterior colporrhaphy until after the removal of the uterus in order to limit blood loss which is logical.

Injury to the rectum will be avoided if the operator directs the penetration of the posterior peritoneum to that point just within the angle made at the uterus by the uterosacral ligaments. Perforation of the peritoneum through an enterocele bulge in this vicinity is quite feasible, but great care must be taken to avoid a high rectocele.

When the posterior cul-de-sac is obscure or difficult to reach, the anterior cul-de-sac should be entered, the cervix amputated (if elongated), and the fundus can then be turned out for digital palpation of the pouch of Douglas and an opening at the most dependent point.

An enterocele, or even a potential one, although it is not a problem so far as the immediate postoperative state is concerned, deserves special mention because of frequent late vault hernias following vaginal hysterectomy. Careful plication of the uterosacral and cardinal ligaments after complete dissection and high ligation of the peritoneal sac have been performed is vital to the success of this operation.

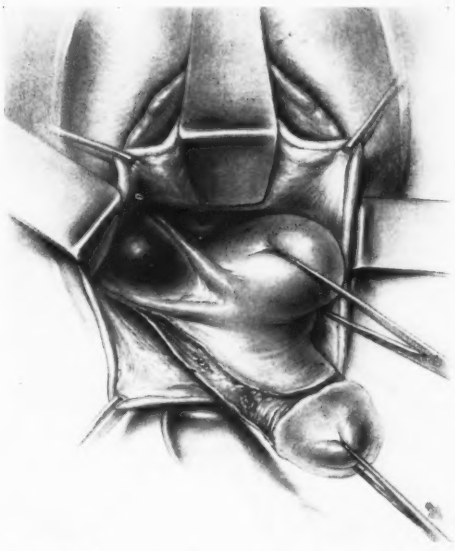

FIG. 10. Undue traction on uterus may cause hematoma in broad ligament (especially right side).

Adequate exposure is essential for vaginal hysterectomy, and certainly some relaxation and descensus are helpful. If the fundus is larger than a 3 months' pregnancy, is irregularly tumorous, or fixed high in the pelvis, the uterus may be exceedingly difficult to remove, even with enucleation of the myomas or morcellation. The excision of tumors lateral to the cervix or fundus can be accomplished generally without undue risk, however, if an incision through the false capsule is made at right angles to the axis of the uterus. If made parallel, large vessels may be cut. Before morcellation is accomplished, the surgeon should be assured that the fundus is free of adherent bowel or adnexa. To secure this condition is not always easy nor certain. Vaginal hysterectomy should probably be abandoned in favor of the abdominal approach if these conditions cannot be met.

COMMENT

From our experience, the mere occurrence of previous major abdominal or vaginal

surgery should not invariably dissuade the surgeon from doing a hysterectomy from below. Nevertheless, it is possible that the initial problem, the type of surgery, the sequelae, and residua will contraindicate vaginal hysterectomy.

Individualization is the key to this problem. It is apparent also that an exaggerated optimism regarding vaginal hysterectomy, especially "semielective" or "combined syndrome" cases, can lead to difficulty when the vagina is narrow or the uterus is fixed with adnexal masses. We agree with Aldrich that the more generous application of vaginal hysterectomy may increase certain technical problems for surgeons. Moreover, candidates for hysterectomy whose symptoms are not logically and obviously related to their internal genitalia should probably be approached from above. Likewise, others who would benefit from exploratory laparotomy, separation of adhesions, and the like, should be operated upon abdominally, inasmuch as even an easy vaginal hysterectomy may not cure the symptoms. Abdominal hysterectomy is still an excellent operation, at times much more suitable than the vaginal procedure, and when there is any doubt the abdominal route should be chosen.

Nevertheless, we believe that the indications for the vaginal operation can be broadened with safety. Our series indicates that, within limits, the average pelvic surgeon in a general hospital can successfully accomplish vaginal hysterectomy under not too rigid indications. Certainly, this procedure has appeal for both patient and operator provided reasonable safeguards are insured.

Although the competent gynecologist should be capable of performing an expeditious vaginal hysterectomy in the majority of suitable cases, he is not required to do hysterectomy from below invariably just to prove he is a capable specialist. Moreover, the fact that this operation can be accomplished by an expert, despite serious handicaps, does not constitute a license for every surgeon to do this procedure. It is certainly possible to practice effective gynecology and rarely do a vaginal hysterectomy.

While many of us are intrigued with vaginal surgery, vaginal and abdominal hysterectomy are not generally truly competitive. "An honest physician," says Stallworthy, "may even declare that in his hands, abdominal hysterectomy is safer than the vaginal operation. His statement should be interpreted as an indication of his personal integrity and operative ability, not as fair comment on the respective merits of these operations." The surgeon must weigh the patient's problems, the findings, and his facility in a decision of operation.

SUMMARY

1. One thousand consecutive vaginal hysterectomies accomplished by surgeons with gynecologic privileges at the Emanuel Hospital, Portland, Oregon, in a 7 year period (1949 to 1956) have been analyzed with regard to surgical difficulties and complications of the first 12 hours following operation.

2. No deaths occurred in this series. The dangerous complications were not numerous but many were avoidable.

3. Hemorrhage was the most critical problem. Despite the fact that two-fifths of the patients required transfusion, most of the blood loss was associated with secondary procedures, usually colpoperineorrhaphy.

4. Other complications—difficult peritoneal entry, injury to the bladder, inability to deliver or remove the uterus, together with excessive bleeding—were related to improper selection of patients, lack of exposure, large or firmly adherent uteri or adnexa, faulty technique, prolonged and additional surgery.

5. Most patients were very well served by vaginal hysterectomy despite the fact that more than one-third had had previous major abdominal or vaginal surgery. Individualization of the case is required, but a previous major abdominal or vaginal operation does not always consitute a contraindication to vaginal hysterectomy.

6. Inflexibility, reckless determination, and exaggerated optimism often impel the operator to pursue a fixed course. More attention to the history and the findings under anesthesia, in the light of the experience of the individual operator, will spare both the patient and the surgeon in vaginal hysterectomy.

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TUMORS OF THE SCAPULA AND CLAVICLE

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TUMORS OF THE SCAPULA and clavicle are of special interest to the orthopedist, the general surgeon, the roentgenologist, and the pathologist, all of whom are likely to be involved in their management. The treatment of tumors in either of these bones has two special characteristics: (1) wide resection is difficult because of the proximity of the thoracic wall, and (2) the more radical resections in this region are crippling and deforming. Since there are no recent comprehensive studies of tumors of the scapula and clavicle, it is hoped that a review of the relevant material in the files of the Mayo Clinic will be of value.

Recent advances in the knowledge of bone tumors made it necessary for us to re-evaluate all such cases pathologically and clinically. Tumors have been included in the study only if material was currently available for adequate pathologic appraisal. In addition to microscopic sections on file in every accepted case, the gross surgical specimen was available for review and for the procurement of new sections in practically all instances.

One hundred and eleven tumors fulfilling these criteria were found to involve the scapula or clavicle. Eighty-eight of these lesions proved, on histologic study, to be primary tumors of bone. The other 23 so closely simulated bone tumors by virtue of actually involving or invading the bone that they are included in this report because of their importance in differential diagnosis. The classification and distribution of the tumors are given in Table I.

The scapula was the site of approximately 70 per cent of the malignant tumors and of almost 90 per cent of the benign. The 3 most common neoplasms of the scapula were osteochondroma, chondrosarcoma, and Ewing's sarcoma. Among clavicular tumors, myeloma, Ewing's sarcoma, and chondrosarcoma led the list. Since only surgical cases in which tissue had been excised were included in this study, the figures do not indicate the true incidence of myeloma in these bones. Nearly 80 per cent of the tumors affecting the clavicle, but less than 60 per cent of those affecting the scapula, were malignant.

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Abridgment of thesis submitted by Dr. Pratt to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

BENIGN TUMORS

Osteochondroma. A benign tumor, the osteochondroma has a bony stalk or core and a cartilaginous cap. Twenty-two patients were found to have such neoplasms, of which only 2 were clavicular. One patient had multiple hereditary exostoses with involvement of both the clavicle and scapula. Fourteen of the 16 scapular tumors which could be accurately localized arose from the anterior surface of the scapula, pushing it posteriorly. In 2 instances, the cartilaginous cap of the osteochondroma was surrounded by a bursa containing loose osteocartilaginous bodies.

All of the patients complained of pain or of swelling, although pain, present in only 9 cases, was a less common feature than in cases of some of the other bone tumors. Roentgenologic efforts produced a correct diagnosis in 13 instances, a far better score than with any of the other types of bone tumor.

Treatment was comprised of excision through the lower portion of the stalk in 15 instances and partial resection of the scapula in 7. Eighteen patients traced for from 18

TABLE I.—TUMORS OF THE SCAPULA AND CLAVICLE

	Benign			Malignant		
Types	*Scapula*	*Clavicle*	*Total*	*Types*	*Scapula*	*Clavicle*	*Total*
Chondrogenic				Chondrogenic			
Osteochondroma*	21	2	22	Chondrosarcoma	13	5	18
Chondroma	2	—	2				
Chondroblastoma	2	—	2				
Hematopoietic				Hematopoietic			
				Myeloma†	4	9	11
				Reticulum cell sarcoma	3	—	3
Unknown origin				Unknown origin			
Mesenchymoma	—	1	1	Ewing's sarcoma	7	6	13
				Mesenchymoma	1	—	1
Osteogenic				Osteogenic			
Osteoid osteoma	1	—	1	Osteogenic sarcoma	5	1	6
Fibrogenic				Fibrogenic			
Fibroma	1	—	1	Fibrosarcoma	4	—	4
Unclassified	1	—	1	Unclassified	1	1	2
Lesions simulating neoplasms of bone				Lesions simulating neoplasms of bone			
Aneurysmal bone cyst	—	2	2	Metastatic carcinoma	4	—	4
Simple bone cyst	1	—	1	Soft tissue tumors			
Eosinophilic granuloma	2†	2	3	Rhabdomyosarcoma	5	—	5
Soft tissue tumors				Fibrosarcoma	3	1	4
Desmoid	3	—	3				
Fibroma	1		1				
Totals	35	7	40	Totals	50	23	71

*One involving both scapula and clavicle.
†One tumor involving both scapulae.

months to 27 years after treatment had no recurrences.

Management of these patients is not difficult. The correct preoperative diagnosis is possible in a high percentage of cases, and if it is not made preoperatively, the gross diagnosis usually is possible at the time of operation. Functional or cosmetic effects and the fear of malignant transformation are reasons for removal of these lesions, and local excision is adequate treatment.

Chondroblastoma. Described by Codman in 1931 and again by Jaffe and Lichtenstein (10) in 1942, benign chondroblastoma has not been reported by others in the shoulder girdle to our knowledge. The 2 chondroblastomas in our series were both in the scapula. One patient was a 14 year old girl who had had pain and swelling for 1½ years; the other was a 31 year old man with symptoms dating back 15 years. Clinical evidence of an active process was present in the younger patient, who had local elevation of temperature, dilatation of veins over the mass, limitation of all shoulder motion, and roentgenographic evidence of destruction near the glenoid. Roentgenograms of the other lesion revealed a cystic area involving practically the entire scapula. In each instance, soft gray-brown and glistening gray tumorous material was curetted. Microscopically, this showed the typical islands of chondroid material in masses of small polygonal cells with occasional giant cells (Fig. 1). Roentgen therapy was directed postoperatively to both tumors. The first patient was alive and well 21 years after operation, and the second was living 9 years after operation but had a relatively large residual mass.

Before operation, it is not possible to distinguish chondroblastomas from malignant bone tumors. The biopsy incision should be placed in such a way that if a tumor requiring radical removal is found, the entire biopsy wound may be removed with the specimen. Microscopically chondroblastomas, which in our experience are always benign, have been confused with chondrosarcomas and malignant giant cell tumors. The importance of a correct diagnosis is underscored by the fact that chondroblastomas nearly always can be controlled by curettage or excision. Although both of

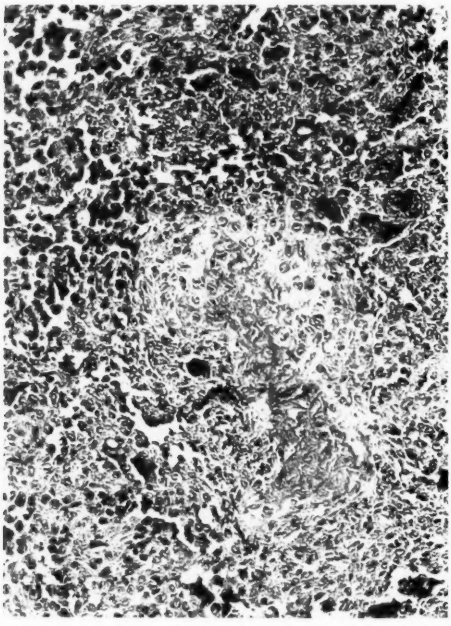


FIG. 1. Benign chondroblastoma of the scapula. Hematoxylin and eosin, ×150.

these tumors in our series received postoperative roentgen therapy, the sarcoma-producing potentiality of such treatment must be borne in mind when treating benign tumors.

Aneurysmal bone cyst. In 1942, Jaffe and Lichtenstein (9) were the first to describe aneurysmal bone cyst. Dahlin and his coworkers (3) reported 26 cases from the clinic in 1955, including the 2 in the present series. Roentgenographically, this lesion commonly appears as an eccentric expansion; and characteristic large, blood-filled channels are found on microscopic examination. The lesional tissue containing the vascular channels often has a prominent benign giant cell component, a fact that has caused confusion of this tumor with bona fide giant cell tumor of bone.

Both of the aneurysmal bone cysts in this study involved the clavicle. One was found in a 17 year old boy and the other in an 8 year old girl. Both patients had had pain and swelling of less than 2 months' duration, and roentgenograms showed expanding tumors of the clavicle in each instance. The patients were alive 3 years and 5 years respectively after treatment, which included partial removal of the tumor and roentgen therapy in each instance. It is extremely doubtful that radiation therapy should be employed for this benign tumor, since cure almost always is effected by surgical removal.

Eosinophilic granuloma. In their microscopic appearance, eosinophilic granuloma, Schüller-Christian disease, and Letterer-Siwe disease seem related processes. This observation was made by Otani and Ehrlich and Jaffe and Lichtenstein (11, 14). Eosinophilic granuloma ordinarily is a solitary process in bone and is easily curable. Schüller-Christian disease is a chronic but diffuse disease that often leads to death of the patient. Most lethal of the 3 is Letterer-Siwe disease, which occurs almost exclusively in infancy and early childhood and has a rapidly fatal course. Differentiation of these 3 syndromes must be made on the basis of the entire clinical picture, the histologic features of a given lesion being nonspecific.

In the present series were 3 examples of eosinophilic granuloma. Two of these involved the clavicle and 1 the scapulae. Ages of the 2 male patients and 1 female ranged from 4 to 36 years. Evidence of a lytic process was seen in the roentgenogram in each instance. One patient treated by radiation after biopsy was well 23 years later. The second had curettage of the lesion followed by radiation and was well 4 years later. In the third patient, a similar lesion developed in the left scapula 12 years after simple surgical removal of a lesion from the right scapula. The right scapular lesion, although asymptomatic, was still demonstrable roentgenographically.

MALIGNANT TUMORS

Chondrosarcoma. Malignant tumors of hyaline cartilage, chondrosarcomas, metastasize relatively rarely or late, but have marked ability to recur locally after surgical re-

moval. The size of the 18 chondrosarcomas in this series varied from 3 by 3 by 7 centimeters to 40 by 35 by 30 centimeters, but most of them had been allowed to grow to enormous dimensions before treatment was sought. Generally, the tumors were so advanced, and had so surrounded and destroyed the scapula or clavicle, that it was impossible to tell whether they originated in the marrow cavity or the cortical region. The tumors were nodular, and their cut surfaces had a characteristic gray, glistening lobulation with areas of cystic degeneration (Fig. 2).

Major contributions to the understanding of the pathology of these tumors were made by Jaffe and Lichtenstein (10, 12, 15) when they classified and described benign chondroblastoma and chondromyxoid fibroma (2 bone tumors which can be confused with chondrosarcoma) and also when they proposed 3 essential microscopic features distinguishing benign from malignant cartilage: (1) the presence of many cells with plump nuclei, (2) more than an occasional cell with 2 such nuclei (Fig. 3), and (3) giant cartilage cells with large single or multiple nuclei or nuclei with clumps of chromatin. These criteria are most helpful in the microscopic assessment of the malignant potential of chondromatous tumors.

The ages of patients with chondrosarcomas ranged from 18 to 66 years, averaging 42 years. There were 11 men and 7 women. The 9 patients not previously treated had had pain or swelling, or both, for from 8 months to 6½ years. The roentgenographic diagnoses were inaccurate in a large percentage of these cases, but with the help of newer advances a correct diagnosis often can be suggested by this means.

Evaluation of the efficacy of treatment administered at the clinic is complicated by the fact that 9 of the 18 patients had had previous treatment. This consisted of excision in 4 cases, biopsy in 2 cases, and aspiration, subtotal resection of the scapula, and radiation in 1 case each.

The forms of treatment employed for these chondrosarcomas at the clinic are listed in Table II. The type of treatment was governed by the location and extent of the tumors when seen. It should be said also that many of the lesions were encountered before the serious long term effects of chondrosarcoma were fully appreciated.

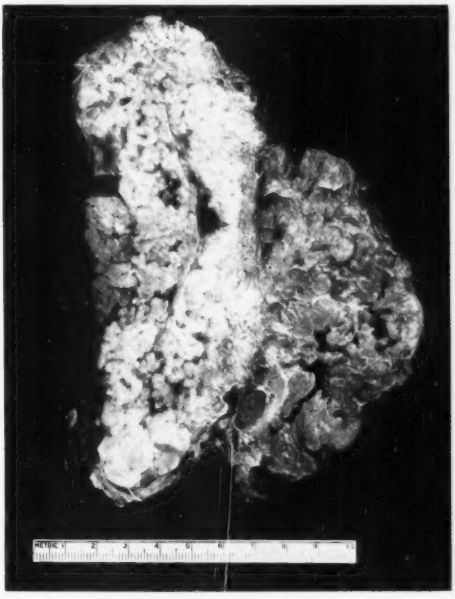


FIG. 2. Chondrosarcoma of scapula showing characteristic lobular appearance of the cut surface.

Additional treatment was employed in 8 patients after unsuccessful initial treatment at the clinic. Fourteen operations for excision of recurrences were necessary in 6 cases. The remaining 2 patients required forequarter amputations after more conservative treatment had failed.

Follow-up data for 5 years or more were available concerning 11 patients treated with

TABLE II.—INITIAL MANAGEMENT OF CHONDROSARCOMA OF SCAPULA AND CLAVICLE AT THE MAYO CLINIC

	Patients
Biopsy or irradiation	2
Palliative resection	1
Excision of recurrent nodules	1
Excision	2
Subtotal resection of the scapula or clavicle	8
Total resection of the scapula or clavicle	2
Amputation of the forequarter	2
Total	18

TABLE III.—INITIAL TREATMENT OF EWING'S SARCOMA OF THE SCAPULA AND CLAVICLE AT THE MAYO CLINIC

	Patients
Biopsy plus x-ray or radium treatment, or both	5
Subtotal resection of clavicle or scapula plus x-ray treatment	5
Total resection of the clavicle or scapula	2
Amputation of forequarter	1
Total	13

hope of cure at the clinic. Six of these 11 patients have survived for 5 years or more. One of these had had no recurrence and was well when last contacted 15 years after operation. Two were well 6 and 7 years after the original surgical operations, although each had had one recurrent lesion excised. Another had had 3 recurrent growths excised and was alive 13 years after the first operation at the clinic, but nodules were palpable in the wound when he was last heard from. The fifth patient in this group survived 9 years despite having had 7 recurrent growths excised. The sixth patient died of unknown circumstances 9 years after the original operation. Of the 5 patients who died during the first 5 years after treatment at the clinic, 4 were known to have had recurrences and 1 died of unknown causes.

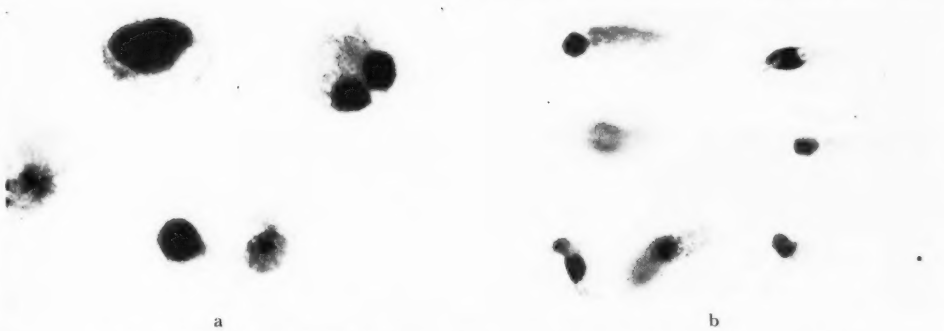
The lethal nature of chondrosarcoma is emphasized by the fact that only 2 of 9 patients treated 10 or more years ago who could be traced were alive; and 1 of these, as mentioned before, had clinical evidence of local recurrence. Recurrent nodules characteristically appear in the soft tissues in the vicinity of the previous operative site. In 1 instance, the ninth recurrence eventuated as a frank osteogenic sarcoma, confirming the observation that occasional chondrosarcomas increase significantly in cellular activity when allowed to recur.

In summary, this series of chondrosarcomas emphasizes that this tumor, although usually reluctant to metastasize, shows a special proclivity for local implantation. It seems probable that with rare exceptions any surgical contact with the tumor, especially cutting into it, will result in implantation of tumor cells capable of growing in the wound. Among the factors that militate against cure is the large size attained by many of these growths before treatment is sought. This, combined with the proximity of the thoracic wall, makes radical extirpation of the tumor without breaking into it difficult, even with forequarter amputation. Some of these tumors are located, of course, in regions where excision of the affected bone accomplishes as radical removal as does forequarter amputation. It seems, however, that the only possibility for improvement in the cure rate lies in performing more radical operations at an earlier time, as advocated by one of us (7). Specimens for biopsy should be taken with the same precautions as are used for biopsy of the breast, so that the larger wound of resection is not contaminated. In the attempt to keep the recurring lesions under control, the same general principle regarding wide excision should be employed as for a primary tumor. This has been advocated by Henderson and one of us (4).

Myeloma. The inclusion of myelomas in this study was due to the fact that biopsy or resection of the mass in the shoulder girdle was the quickest and easiest method of arriving at a diagnosis. Only 4 of the 11 myelomas were solitary lesions of the shoulder girdle when first seen. Of these 4, 2 had developed to advanced status within 3 years; in the other 2 cases, the patients had been traced less than 2 years from the time of diagnosis.

Reticulum cell sarcoma. Parker and Jackson described reticulum cell sarcoma of bone in 1939. The 3 tumors of this type in our series were located in the scapula. All of the patients were males, and their ages ranged from 11 to 66 years. All of them complained of pain which had been present for periods up to 1½ years. Destruction of bone was evident on the roentgenogram in each instance.

After biopsy, curettage, or excision of the tumor led to the diagnosis, radiation therapy was employed in each case. No comment regarding the efficacy of treatment is warranted in this small series with relatively short follow-up period. It is important, however, because of the better over-all prognosis of



a b

FIG. 3. a, Relatively anaplastic chondrosarcoma; nuclei are large. and many cells contain more than one nucleus. Hematoxylin and eosin, ×550. b, Chondroma illustrating cells with typical single, small nuclei. Hematoxylin and eosin, ×550.

reticulum cell sarcoma, that it be distinguished from Ewing's sarcoma and myeloma. Parker and Jackson noted that 13 of their original 17 patients were alive 6 months to 14 years after treatment.

Ewing's sarcoma. First described by Ewing in 1921, the sarcoma named for him is composed of small cells uniform in size and shape. More recently, it has been extensively studied by McCormack and co-workers (16, 17). Geschickter and Copeland discussed 167 cases of Ewing's sarcoma and mentioned briefly an atypical form with cells of somewhat larger size. In the present series 13 Ewing's sarcomas were encountered. Nine of these tumors were composed of typical, uniform small cells with practically no intercellular substance; and 4 of them were of a similar structure but composed of cells that were slightly, yet definitely, larger in size. Complete gross specimens of 8 of these 13 Ewing's sarcomas were available for study. The configuration indicated an origin in the medullary cavity of the bone in most instances, the cortex being commonly expanded and perforated by the tumor.

Ages of the patients in this group ranged from 7 to 36 years, with an average of 21 years. There were 7 males and 6 females. Pain or swelling had been present for from 4 days to 10 months. A malignant process was suggested in the original roentgenographic diagnosis in 5 instances, whereas other interpretations included cystic lesion, roughening of the bone, periosteal tumor, and rarifying osteitis.

Two patients had received roentgen therapy previously. The treatment employed at the clinic is summarized in Table III.

The prognosis for Ewing's sarcoma was poor. Nevertheless, 1 of the patients who had a tumor of the clavicle that measured 5 by 4 by 3 centimeters was alive and well 28 years after total excision of the tumor followed by local roentgen and radium therapy. The other 12 patients in this group succumbed within 3 years. The available data do not allow a dogmatic stand regarding the treatment of choice for Ewing's sarcoma. McCormack and associates found no significant difference in the prognosis of patients treated surgically and those treated primarily by radiation.

Osteogenic sarcomas. Highly malignant, osteogenic sarcomas are likely to metastasize early. The histologic diagnosis of this tumor is based on the finding of osteoid produced by malignant cells. Five year survival rates of patients having tumors with such histologic qualifications as these have been reported by Coventry and Dahlin as 19 per cent, and by Jaffe (8) as less than 10.

In general, the osteogenic sarcomas in this series were smaller than the chondrosarcomas; their size varied from 5 centimeters in diameter to measurements of 14 by 14 by 7

TABLE IV.—MISCELLANEOUS LESIONS

	No. cases
Chondroma	2
Mesenchymoma	2
Osteoid osteoma	1
Fibroma	1
Unclassified	3
Simple bone cyst	1
Metastatic carcinoma	4
Locally occurring soft tissue tumors	13
Total	27

centimeters. All of them had destroyed the cortex of the affected bone and invaded the adjacent soft tissues. Except for one growth which grossly resembled a chondrosarcoma, the bulk of each tumor consisted of gray fibrous material with a gritty cut surface.

The patients were 3 men and 3 women whose ages ranged from 24 to 54 years. Symptoms of pain or swelling had been present from 3 weeks to 20 months in 5 of them, whereas the sixth had had local pain for more than 5 years. A malignant process was suggested by the roentgenogram in 4 cases.

Treatment prior to arrival at the clinic consisted of roentgen therapy in 3 instances and subtotal resection of the scapula in 1. Initial treatment at the clinic consisted of local excision of 1 of the lesions and, owing to erroneous diagnoses, roentgen therapy to 2 others. Of the remaining 3 patients, 2 underwent forequarter amputations and 1 had total resection of the scapula; but this last patient required forequarter amputation for recurrence 2½ years later.

The dismal outlook for patients with osteogenic sarcoma of the shoulder girdle is emphasized by this group of cases, 5 of whom were dead within the first 5 years after initial treatment at the clinic. One of the 6 was alive 1 year after a forequarter amputation. No conclusions regarding treatment for osteogenic sarcoma can be based on this small group of cases. It seems obvious, however, that more radical and earlier surgical treatment of this radioresistant tumor is necessary if the results are to be improved.

FIBROSARCOMA

Lichtenstein (13) has discussed fibrosarcoma as a malignant tumor which can arise within a bone. It is difficult to distinguish from fibrosarcoma of soft tissues which has involved bone secondarily. The 4 tumors in this group involved the scapula. The average age of the 3 men and 1 woman was 33 years. The usual complaints of pain and swelling were presented. The roentgenogram showed destruction or involvement of bone in each instance. The fibrosarcoma in 2 patients was considered inoperable when they were first seen, and they were treated with radiation or Coley's toxins after biopsy. The third patient had recurrent nodules removed, having had previous local excision elsewhere; and the fourth was treated by total resection of the scapula. The 4 patients died at intervals of 1, 2, 3, and 4 years after treatment at the clinic. In 2 cases, distant metastasis was known to have occurred.

MISCELLANEOUS LESIONS

Only a brief discussion of this group (Table IV) is presented because the lesions were not primary tumors of bone or because the number of cases was small.

The 2 chondromas were periosteal in location, and both patients were well and without recurrence 20 years after initial treatment.

Two tumors were classified as mesenchymomas because they were made up of several tissues. The first was benign and arose from the outer end of the clavicle or the acromioclavicular joint of a 60 year old woman. Numerous miniature and misshapen bones were present in a fatty stroma. The second tumor involved the scapula of a 58 year old man. Four years after resection of the scapula, pulmonary lesions with an identical microscopic appearance developed. These consisted of a mixture of osteogenic sarcoma, chondrosarcoma, and tissue that greatly resembled malignant synovioma.

The single osteoid osteoma was located in the neck of the left scapula of a 6 year old boy who had severe pain in the arm associated with atrophy of the arm.

A benign fibroma occurred in the left scapula of a 32 year old man. It had pro-

duced a large area of destruction evident roentgenographically. Tissue removed for biopsy was erroneously regarded as giant cell tumor, but roentgen therapy led to complete sclerosis of the lesion within 6 months.

Three tumors could not be classified satisfactorily, although material appeared to be adequate for histologic study.

The simple bone cyst, metastatic carcinomas, and soft tissue tumors involving the scapula and clavicle were included in the over-all statistics because prior to surgical exploration and biopsy these lesions appeared to be primary tumors of bone. The number of metastatic carcinomas is unduly small because only those lesions subjected to surgical treatment are included in this series.

COMMENT

A wide variety of lesions may involve the clavicle or scapula either primarily or secondarily, but certain tumors of bone were not found in the clavicle or scapula in this series. These include chondromyxoid fibroma, parosteal osteogenic sarcoma, benign giant cell tumor, malignant giant cell tumor, adamantinoma, liposarcoma, hemangiomatous neoplasms, and chordoma.

Certain benign lesions requiring conservative treatment, such as benign chondroblastoma, eosinophilic granuloma, and aneurysmal bone cyst, clinically may simulate lesions such as chondrosarcoma which require radical resection. Also, certain malignant growths which often are best treated without radical surgery, such as myeloma, Ewing's sarcoma, and reticulum cell sarcoma, may be confused clinically with lesions requiring ablation. Therefore, adequate material must be obtained for study before proceeding with treatment. A specimen of the tumor should be taken in such a way that the wound produced during a subsequent resection will not become contaminated by tumor cells. The sample of the tissue selected for biopsy must be representative. For example, if only a portion of an aneurysmal bone cyst is submitted, an erroneous diagnosis of giant cell tumor may seem correct to the microscopist. Malignant cartilaginous tumors may have large regions with insufficient histologic alteration to prove that they are chondrosarcomas. With minute specimens the differentiation of an inflammatory process from reticulum cell sarcoma or myeloma may be impossible.

More radical and earlier surgical treatment is necessary for improvement of the prognosis for patients with radioresistant lesions such as chondrosarcoma, osteogenic sarcoma, and fibrosarcoma. Radiation is probably the treatment of choice for reticulum cell sarcoma and Ewing's sarcoma of the shoulder girdle. Benign lesions must be correctly categorized lest they be overtreated.

SUMMARY

One hundred and eleven tumors involving the clavicle and scapula, seen at the Mayo Clinic over a 50 year period, were studied clinically and pathologically. Eighty-eight (80 per cent) of these were primary tumors of bone and the remainder were lesions which closely simulated primary bone tumors. The 4 most common bone tumors were osteochondroma, chondrosarcoma, Ewing's sarcoma, and myeloma.

Primary bone tumors of the scapula were more than twice as common as those of the clavicle, and the majority of tumors involving the scapula and clavicle were malignant.

Adequate biopsy is necessary in the determination of which of these tumors is malignant and which of the malignant ones are best treated by radiation. Earlier, more radical, and well planned treatment is necessary if the dismal outlook for patients with radioresistant tumors of these bones is to be improved.

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THE INHIBITORY ROLE OF THE PYLORIC ANTRUM ON THE CEPHALIC PHASE OF GASTRIC ACID SECRETION IN DOGS

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IN A PREVIOUS PUBLICATION (5) we showed that the pyloric antrum, when left in continuity with a 50 per cent residual gastric pouch, protected dogs against histamine-induced peptic ulceration. A number of theories were proposed and experiments devised to elucidate the modus operandi of this apparent protective role of the pyloric antrum. In the present article are reported in a preliminary way some of the observations we have made on this problem to date.

METHOD

Experiments were carried out on 3 young healthy mongrel dogs. As the first step, in each animal isolated antral and Pavlov pouches were made. Into each pouch a flanged stainless steel cannula was inserted and brought out through a separate stab wound in the skin. The antrum was measured from the incisura angularis to the pyloric ring, and the Pavlov pouches were made as large as possible to insure inclusion of a significant segment of the acid-secreting mucosa. The animals were allowed approximately 2 months to recover, at which time the rate of secretions of the Pavlov pouches were well established.

Throughout these experiments, the animals' health appeared to be good, and observations were made only if the animal did not develop any untoward symptoms, such as nausea or vomiting, during the experiments.

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Each test was commenced 20 to 24 hours after the previous meal and after 1 hour of collection of the secretions of the Pavlov pouch under basal conditions on the day of the proposed experiment. The gastric secretion was stimulated by the ingestion of meat. The juice was collected routinely postprandially every hour, for 4 hours during each experiment. At least a day was allowed between each test, and each test was repeated 2 or more times on each dog. The volume of each sample of juice was measured and the concentration of free acid determined by titration with 0.1 normal sodium hydroxide using Töpfer's reagent as the indicator. The output of each pouch was calculated from these values as milliequivalents of acid secreted per hour. Three sets of experiments were devised.

Experiment 1—control. The dog was given 200 grams of fat-free beef heart boiled in 200 cubic centimeters of tap water for 15 minutes. The amount of food and liquid given was accurately measured. Collections were then taken from the Pavlov pouch. The pyloric antrum was left undisturbed.

Experiment 2—saline control. The details of the experiment were the same as in experiment 1 but differed in that following the ingestion of the food, warm normal saline solution was introduced into the antral pouch until the pouch was filled without overdistention. The antral cannula was then stoppered. At the end of each hour of collection the cannula in the antral pouch was inspected, and when necessary fresh saline solution was added to keep the level of the solution in the cannula at the same height

TABLE I.—AVERAGE HOURLY SECRETION AND AVERAGE TOTAL QUANTITY OF SECRETION AFTER 4 HOURS FROM PAVLOV POUCH FOLLOWING NO IRRIGATION, CONTROLLED SALINE IRRIGATION, AND ACID IRRIGATION OF THE ANTRAL POUCH

Dog No.	*Experiment*	*Average hourly secretion of Pavlov pouch after test meal, mEq./l.* 1	2	3	4	*Average total quantity of Pavlov pouch secretion for 4 hrs. after test meal, mEq./l.*
50	1. Control	8.97	6.42	1.06	0.92	17.37
	3. Acid in antral pouch (5 exp.)	3.33	2.29	1.36	1.01	7.99
22	1. Control (4 exp.)	5.25	3.76	3.07	1.64	13.58
	2. Saline control (6 exp.)	2.83	2.35	1.16	0.17	6.34
	3. Acid in antral pouch (8 exp.)	1.67	0.78	0.22	0.15	2.89
46	1. (3 exp.)	5.58	3.84	3.27	1.63	14.18
	2. (7 exp.)	2.81	3.05	1.61	0.61	8.40
	3. (8 exp.)	1.87	1.83	0.43	0.15	4.28

as obtained at the beginning of the experiment.

Experiment 3. The details were again similar to the control in experiment 1. In these experiments, however, at the time the animal was given its food 0.1 normal hydrochloric acid was introduced into the antral pouch until the pouch was gently filled and the solution rose in the antral cannula stem. The cannula was then stoppered and was checked at each hour as collections from the Pavlov pouch were obtained. Further 0.1 normal hydrochloric acid was only added to bring the level in the cannula back to the same level as it was at the beginning of the experiment. In all, 41 observations were made in the 3 dogs.

OBSERVATIONS

From Figure 1, one can see that the installation of acid into the antral pouch caused marked inhibition of the secretion of the Pavlov pouch. The degree of inhibition varied but this pattern was seen in all experiments except on 2 occasions. The amount of acid secreted by the gastric pouch did not change on one occasion and increased slightly on the other. In experiments on 2 dogs in which saline solution was introduced into the antral pouch, it too produced a decrease in the acid secretion of the indicator pouch but to a much lesser degree than when 0.1 normal hydrochloric acid was used.

In Table I the average hourly amounts of acid secreted by the Pavlov pouch after the ingestion of a test meal as well as the average total amounts of acid secreted during the 4 hour postprandial period are given. Analysis of these data show that the introduction of acid into the antrum resulted in reduction of the average total quantity of acid secreted by the Pavlov pouch during each of the 4 hour periods after the meal compared to control values. The maximum degree of reduction appeared to occur in the first 2 hours of collection and in dogs 22 and 50 during the second hour of collection particularly. As one compares the average total amount of acid secreted during 4 hours in these experiments, it is apparent that the percentage of the reduction is significant when acid was introduced into the antrum compared to control values when the antrum was left undisturbed: i.e., dog 50, 55 per cent reduction; dog 22, 79 per cent reduction; and dog 46, 70 per cent reduction.

DISCUSSION

These experiments indicate that the introduction of 0.1 normal hydrochloric acid into isolated antral pouches exerts a significant inhibitory effect on the acid secretion of a Pavlov pouch stimulated by the ingestion of food. It is usually accepted that the gastric secretory response by the Pavlov pouch to the sight, smell, or ingestion of food represents the cephalic phase of gastric secretion and is mediated via the vagal nerve

fibers. This is particularly true for the first 2 hours of collection after the administration of a test meal.

In these experiments, since the antrum was isolated and not stimulated, the liberation of gastrin could not have played a significant role in the stimulation of the gastric juice. The fact that acid introduced into the antrum could reduce the quantity of secretion by the Pavlov pouch under these experimental conditions would indicate that the mode of action in the antrum must be through some means other than inhibition of gastrin release. Dragstedt (6, 7) and his co-workers have thought from their experiments that acid in the antrum acts primarily by inhibiting gastrin release. That this may not be the only way in which acid in the antrum may depress gastric secretion seems likely from these experiments.

Another explanation as to the action of acid in the antrum on gastric secretion is that nerve impulses arising from the antrum after acid is introduced could reflexly decrease the acid secretion in the Pavlov pouch by their effect on transmission of nerve impulses via the vagus nerve. Code and Watkinson have shown that the inhibition response of the secretion of gastric pouches to the introduction of acid in the duodenum depends upon the presence or absence of the vagal fibers to the indicator pouches. When the vagal fibers are intact inhibition of gastric secretion occurs. When the pouch is vagally denervated no such inhibitory influence of secretion by the introduction of acid in the duodenum appears. The fact that the antrum was completely isolated from the stomach in these experiments is against this concept; still this theory cannot be completely evaluated by these studies until further observations are made when the antrum and indicator gastric pouches are autotransplanted to the subcutaneous tissues. Experiments of this kind are being carried out in our laboratory at the present time.

An additional plausible explanation for our observations, we believe, is that a humoral factor capable of inhibiting further gastric acid secretion is elaborated when acid comes in contact with the antrum mucosa. The published works of Brunschwig and associates, Jordan and Sand, and Harrison and his co-workers also lend strong support to this concept. There is a precedent for gastric secretion inhibition by a hormone in enterogasterone which is liberated when adequate concentrations of fat or sugar come into contact with the mucosa of the upper small intestine.

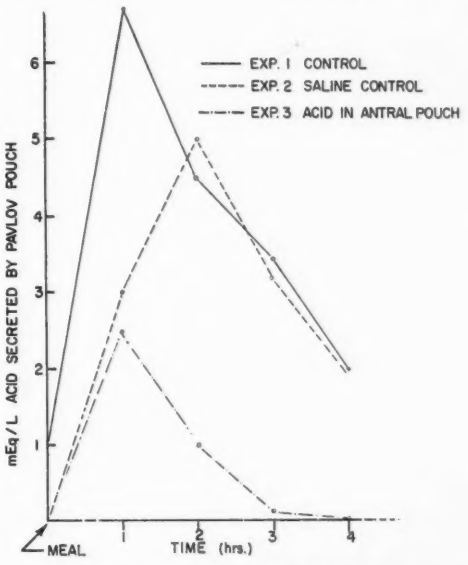

FIG. 1. Typical response of a Pavlov pouch following acid introduction into the antrum. This is to be compared with the control when no irrigation was used and when saline was used to irrigate the antral pouch.

Much remains to be learned about the function of the antrum. As experimental evidence accumulates it becomes clear that the antrum plays a dual role. It is capable of stimulating gastric acid secretion by the formation and release of gastrin and may inhibit gastric acid secretion by an as yet unidentified inhibitory mechanism invoked when acid in sufficient concentration comes into contact with the antral mucosa. The relative significance of these two functions

in animals and man also remains to be studied. The fact that the antrum, when left in continuity with the residual gastric pouch so that acid may come in contact with its mucosa, may inhibit further gastric secretion lends strong experimental support to the use of segmental gastric resections in the surgical treatment of medically resistant duodenal ulcer.

SUMMARY

In dogs, the introduction of 0.1 normal hydrochloric acid into isolated antral pouches inhibited the secretion of the Pavlov pouch in response to a standard meal (cephalic phase of gastric secretion). The possible mechanisms of this inhibitory action by acid in contact with antrum mucosa has been discussed. It appears that the inhibition may be brought about by mechanisms other than the interference with the formation or release of gastrin.

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THE TRANSABDOMINAL REPAIR OF HIATAL HERNIA

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RECENT REPORTS of repair of hiatal hernia have stressed the thoracic approach. The author believes that an abdominal approach can be as effective as the thoracic route and is a more desirable operation in many patients. Since the operation is usually performed on patients in the middle and older age groups, the procedure should consume the least time possible, be the least traumatic, afford ample opportunity to explore the abdominal organs, and permit the smoothest postoperative course. To this end a simple technique for repair through the abdomen has been used, and patients even in the eighth decade of life have tolerated the procedure with minimal postoperative complaints and morbidity.

ANATOMIC CONSIDERATIONS

Hiatal hernia is a sliding hernia into the posterior mediastinum. It contains its own sac and lies in the thorax without entering the pleural cavity. The sac usually contains the stomach cardia but other abdominal viscera may be in the sac, particularly the colon, omentum, small intestine, and upper pole of the spleen.

Most authors believe that the most common form of this hernia is the sliding "short esophagus" type (Fig. 1A), in which the esophagus appears short but is actually of normal length with its distal end above the diaphragm. In the less common parahiatal or paraesophageal hernia (Fig. 1B), the esophagus is of normal length, and its distal end together with the stomach cardia is held beneath the diaphragm by a few strands of diaphragm muscle.

The final form of the hernia, the rare true short esophagus (Fig. 1C), is accepted by all to be exceedingly uncommon. In this type of hernia, the thoracic portion of the stomach may lack a sac.

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Factors in the hernia formation include congenital weakness of the muscular diaphragmatic tissues which form the hiatal ring, loss of tissue resilience as a result of advancing age, and sudden increase in the positive intra-abdominal pressure enhancing the negative intrathoracic pressure with its constant upward pull on the stomach. Any factor increasing the intra-abdominal pressure may precipitate the acute attack.

Like inguinal hernia, the hiatal hernia is due to congenital weakness from birth, but usually does not appear until adult or late life. Relationship has been shown to exist between hiatal hernia and the female sex, obesity, age, and pregnancies by Rigler and Enebo. Reflex esophagus shortening, with hernia formation, has been accorded to gallbladder disease, to peptic ulcer and pancreatitis, and to nervous reflex caused by external stimulus.

SYMPTOMS

The great majority of these patients have no symptoms or minimal symptoms that are gastric in nature. These include epigastric or substernal pain or discomfort, usually after meals, simulating peptic ulcer, gallbladder disease, pancreatitis, or esophageal disease. Frequently the hernia is found as an incidental finding in x-ray studies, particularly if the roentgenograms have been taken with the patient in the Trendelenburg position.

A small percentage of patients have severe complaints. If the predominant picture is thoracic, the patient has dysphagia or chest pain, with radiation of the pain into the back, to the precordium, or into both arms or shoulders simulating heart disease. With the dominant picture abdominal,

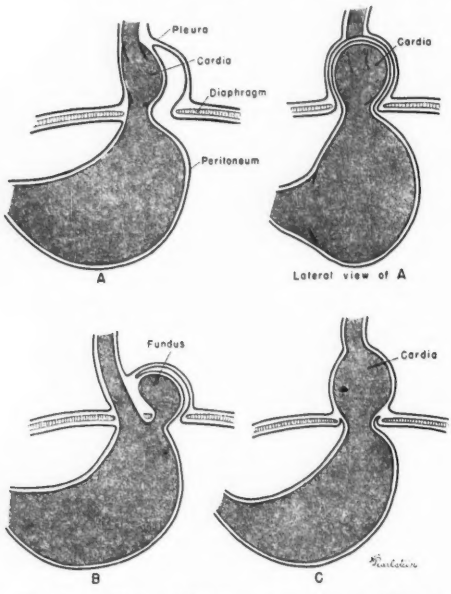

FIG. 1. A, Sliding "short esophagus" type of hernia. The esophagus is of normal length with its distal end above the diaphragm. This is considered the most common type of hiatal hernia. The sac is usually to the left and anterior to the stomach. B, Parahiatal or paraesophageal type of hernia. Normal length esophagus with its distal end beneath the diaphragm. A few strands of diaphragm muscle hold down the esophagus and cardia. C, Rare true short esophagus. In this type the sac is usually missing.

there is subxiphoid or epigastric pain with radiation to the back. Vomiting and belching are prominent in both forms and may occur after each meal. Pain usually occurs after food ingestion, particularly a large meal, and relief is obtained by self-induced vomiting, assumption of a sitting position, or walking. As a result, many patients limit their diets to light meals, mainly fluids, and sleep in a semisitting position.

Ulceration may occur in the area of the stomach constriction with gross or microscopic bleeding causing severe anemia. In some instances, patients with gastric bleeding have both duodenal ulcers and hiatal hernia. This will confuse the picture, but it is our observation that in most of these cases the patient bleeds from the ulcer rather than the hernia. Incarceration or strangulation of the hernia occurs with the prominent sign of a severe, acute increase of the pain.

TECHNICAL CONSIDERATIONS

Most patients respond well to symptomatic therapy. When symptoms are severe, operative intervention must be employed. In certain selected cases of poor risk or very old people, phrenic nerve block or excision may be used successfully when bronchiectasis is not present on the left side. However, this procedure should be used only in those patients who the surgeon believes would not be able to withstand a major procedure.

I employ the abdominal approach in the majority of patients who do not have a true short esophagus. Help is obtained in making this diagnosis by using oblique views of the esophageal barium studies. Frequently an oblique view will show an esophagus of normal length which appears short on the usual anterior posterior views.

The abdomen is entered through a left paramedian or a midline incision which is extended upward as far as possible to the left of the xiphoid. It is necessary to obtain all the exposure possible through the upper angle of the incision. The gallbladder rest is raised to hyperextend the patient. After survey of the abdomen, the left lobe of the liver is released by severing its coronary ligament. This ligament is usually bloodless but care should be taken as the midline is approached not to injure the hepatic veins as they enter the vena cava. The left lobe of the liver is retracted medially and anteriorly.

At this time the esophageal hiatus and its contents come into view. The hernia usually contains the stomach cardia which lies anterior to a transversely flattened esophagus. Frequently the upper pole of the spleen enters the hernial sac. The spleen can be reduced easily but it is found that there is a shortening and thickening of the gastrosplenic ligament, so that the spleen is fixed close to the stomach and to the hiatal aperture. If the spleen is a mechanical hindrance, it may be advisable to remove it

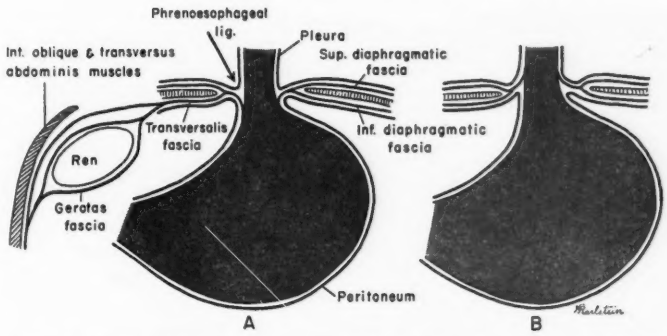

FIG. 2. Phrenoesophageal ligament consisting of extension of the superior and inferior diaphragmatic fasciae next to the close-lying peritoneum and pleura. Some think that this is an extension of the transversalis fascia as it reflects off the posterior surface of the transversus abdominis muscle and the Gerota fascia. Extending from the diaphragm to the esophagus, with variable fixation to the esophagus, it may extend downward into the abdomen or upward into the mediastinum in a conelike fashion, depending on the movement and position of the esophagus and stomach and the state of attenuation of the ligament.

early in the operative procedure before it is torn.

The stomach is decompressed by means of the Levin tube that has been passed preoperatively, and the hernia contents are reduced with gentle traction. Adhesions between the stomach wall and the hiatal ring can be divided under direct vision by blunt dissection and, if necessary, can be severed with a long scissors.

The hiatal opening is found to be a half elliptic opening with its apex superior, to the left, and anterior, while its base extends posteriorly, caudad, and to the right toward the vertebral bodies. The size of the hiatal aperture varies but usually admits from two to four fingers. The hernial sac enters and lines the hiatus. The esophagus lies as a transversely flattened organ in the posterior compartment of the hiatal aperture and slightly to the right (Fig. 3B).

The lower end of the esophagus is then separated from its bed while slight traction is kept on the stomach with Babcock clamps. This is done by incising the hernial sac to the left of the esophagus or rupturing through the sac bluntly at that area with the forefinger. In either case the esophagus is freed from its bed by using the forefinger, proceeding from the left to the right side. The esophagus should be well liberated for a distance of fully 1 to 2 inches. A Penrose drain is placed around the esophagus for traction (Fig. 4).

During this maneuver the phrenoesophageal ligament described by Allison, Madden, and Johnsrud with its overlying peritoneum and pleura may be partially ruptured, depending on its position and state of relaxation (Fig. 2).

The phrenoesophageal ligament is a ligamentous attachment from the esophagus to the diaphragm. Its origin is thought to be from the superior and inferior diaphragmatic fasciae, primarily the superior. Some think that it is a continuation of the transversalis fascia as it reflects off the posterior of Gerota's fascia and the posterior aspect of the transversus abdominis muscle. The ligament, frequently well formed and encased by the close-lying peritoneum and pleura, projects upward as a cone into the mediastinum or downward into the abdomen depending upon the movement and position of the esophagus and diaphragm and its own state of attenuation brought about by the hernia. It also has varying degrees of attachment to the esophagus, in some cases being

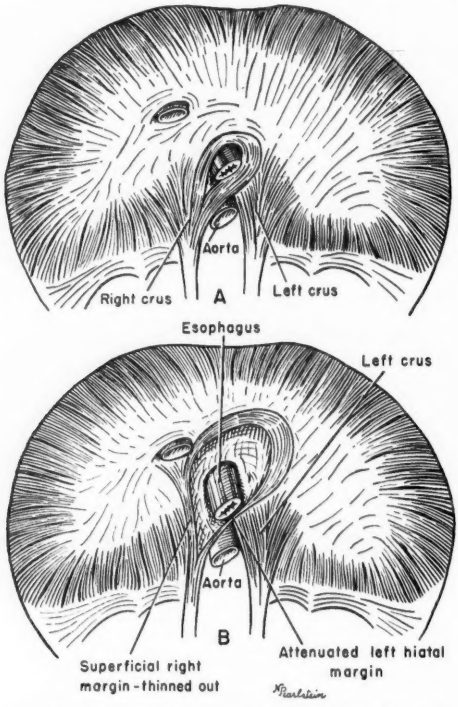

FIG. 3. A, Shows the normal hiatal orifice with both margins arising from the right crus of the diaphragm. This crus separates into a superficial muscle which forms the right margin of the hiatus and into a deep muscle which forms the left margin of the hiatus. The hiatus has a crater-like appearance with its apex toward the mediastinum and posteriorly. B, Shows attenuated fibrous band extending over the aorta to form the posterior margin of the hernia. This is frequently the appearance when the hernia is large.

intimately attached to the esophagus and in others less so. Its degree of fanning out at its point of attachment to the esophagus also varies. It is this ligament that Allison and Johnsrud claim should be sutured to the underside of the diaphragm and that Madden has sutured to the upper side of the diaphragm.

Up to this stage of the operation bleeding is minimal. The base of the sac, now partially severed, is around the cardia of the stomach, and the distal or cephalad portion of the sac with the phrenoesophageal ligament proceeds up into the mediastinum from the hiatal aperture. Part of all of the remaining sac cephalad is resected by raising its free edge and dissecting up around it into the mediastinum with a long Kelly clamp, keeping the concavity of the clamp curve constantly toward the sac lumen so as to avoid unnecessary damage to the mediastinal tissues. To carry out this procedure it is necessary to have extra long instruments including the needle holder, scissors, Kelly clamps, and forceps.

The denuded muscular edges of the diaphragm around the hiatal aperture are grasped with long Kelly clamps and pulled toward the operator. Interrupted heavy No. 2 silk sutures are employed to approximate the edges of the diaphragm by starting at the left angle of the aperture and proceeding toward the esophagus. The first suture placed is used for traction. If sufficient tissue is present overlapping is done; however, this is not necessary for a good result. Usually both edges of the aperture have good muscle fibers, but it is possible for the anterior or the posterior lip to consist of a thin fascial layer. If this is true in the anterior lip, sutures must be placed carefully because they are being inserted through the fascial layer directly beneath the inferior portion of the pericardial sac.

In the majority of cases complete repair can be obtained by displacing the esophagus to the right and posteriorly. In some instances the hiatal defect seems to extend to the spinal column. This appears to be a herniation into the aortic opening but there is usually a fibrous band extending over the aorta to form the margin of the hernia (Fig. 3). In this type it is necessary to place sutures posterior to the esophagus.

Both right and left margins of the diaphragm aperture about the esophagus are from the right crus of the diaphragm, and not from both crura as was commonly thought. The right margin consists of a thin superficial layer from the right crus, and the left margin of the hiatus consists of a thick deep muscle from the same crus (Fig. 3). This has been pointed out by Carey and

Hollinshead and emphasized by Madden.

If the defect cannot be fixed by approximation, a new esophageal hiatus can be made with a plastic slip from the hiatal ring, or the esophagus can be transplanted by incising the hiatal ring and using tantulum mesh over the original aperture. If, at operation, it is found that the esophagus cannot be brought beneath the diaphragm the cardia of the stomach is sutured to the hiatal margins. Finney pyloroplasty for this type of short esophageal hernia has been described by Burford and Lischer in 16 patients with excellent results.

The actual closure of the diaphragm about the esophagus should be carefully evaluated. The aperture, when repaired, should admit the small finger alongside the esophagus. To close the aperture further may produce symptoms of dysphagia later when periesophageal fibrosis takes place with some constriction. To leave the aperture wider may invite recurrence. The esophagus is not sutured to the new ring, but sutures can be placed between the stomach cardia and the diaphragm. A drain is placed only if the spleen has been removed. Postoperatively the stomach is decompressed for 2 days and the patient is supported with intravenous therapy.

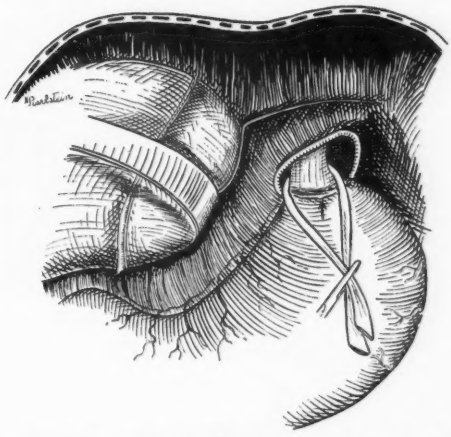

FIG. 4. Shows left lobe of the liver retracted and cuffs of the severed hernial sac around the gastric cardia and around the margin of the hiatal aperture. An attempt is made to excise the sac cephalad. Esophagus should be well liberated for a distance of 1 to 2 inches.

DISCUSSION

Results in 16 patients operated on with this technique during the past 2½ years have been excellent. The oldest patient in this group was 73 years of age. Several patients had large hernias nearly the size of a grapefruit. Of these, 2 patients who were first seen with acute incarceration had very large hernias.

All patients had mild postoperative courses without complications, with minimal postoperative pain or discomfort, and with no mortality. One patient had a recurrence of dysphagia 6 months after surgery. Esophagoscopy did not reveal esophagitis or ulceration, but rather a fixation around the distal end of the esophagus external in origin. Following 2 dilatations this patient has been symptomless. In 1 patient a subtotal gastrectomy and a hernia repair were done at the same time when it could not be determined whether his gastric bleeding was due to the duodenal ulcer or to a large hiatal hernia.

With this procedure a periesophagitis is obtained which fixes the lower end of the esophagus and upper end of the stomach eliminating, to a large extent, the previous sliding effect. This was seen in 1 patient when routine postoperative roentgenograms showed a small recurrence of the hernia but the patient was completely symptomless. Postoperative x-ray studies of the other patients did not reveal the recurrence of hernia. There was no apparent occurrence of postoperative esophagitis.

The phrenoesophageal ligament is not as easily identified from below the diaphragm as it is from above, and we did not rely on its use as described by others. This ligament cannot be isolated and grasped from below the diaphragm as it can from above. This is especially true when the hernia is large since the tissues are more attenuated.

When the muscular fibers of the hiatal edges of the diaphragm are stripped and

sutured a good fibrosis is obtained, such as is observed when the external oblique muscle and the internal oblique muscle are sutured to Poupart's ligament in inguinal hernia.

SUMMARY

1. The indications for and advantages of a transabdominal repair of hiatal hernia are described.

2. The technique and anatomy of the repair and the results in 16 patients are presented.

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STUDIES OF CEREBROSPINAL FLUID PRESSURE DURING HYPOTHERMIA IN INTRACRANIAL SURGERY

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EXPERIMENTAL STUDY in animals has indicated that decreases in brain volume and cerebrospinal fluid pressure occur with hypothermia. Cerebrospinal fluid pressure measurements during intracranial operation have revealed a fairly uniform pattern of initial increase with induction of anesthesia and intratracheal intubation in a variety of cerebral lesions. When these cerebrospinal fluid pressure measurements were correlated with observations made during operation under hypothermia, the findings suggested that the method of hypothermia employed with the surgery did not afford a practical method for reducing markedly increased intracranial pressure secondary to space-occupying lesion.

MATERIAL AND METHODS

In one hypothermia technique a mattress was used which contained a continuous coil mechanism through which a solution of alcohol was pumped. The patient was wrapped in the mattress and cooling was obtained by refrigeration of the alcoholic solution in the coils of the mattress. The machine could also warm the circulating alcohol and thereby rewarm the patient. In the other technique the patient was packed in ice contained in rubber sheets and was removed from the ice packs when his rectal temperature reached 30 to 31 degrees C. The mattress generally permitted more accurate control of the body temperature, since the warming and cooling mechanism was available during the entire operative procedure.

The patients were prepared for hypothermia with 25 to 50 milligrams of intramuscular chlorpromazine at bedtime and 25 to 50 milligrams of chlorpromazine and 0.3 to 0.4 milligram of atropine sulfate preoperatively. Intravenous sodium pentothal and succinylcholine chloride were used during induction and intubation, and following this the patients were maintained on ether, nitrous oxide, and oxygen inhalation through a closed system with supplementary intravenous succinylcholine chloride. A cardioscope permitted check on possible cardiac abnormalities during operation. Temperature was recorded with a rectal thermocouple.

A continuous Tuohy spinal catheter, 3.5 French, was inserted either before or after intratracheal intubation into the lumbar intrathecal space and attached to a spinal fluid manometer. The level of exit of the catheter from the back represented the zero line on the manometer.

Observations were made during intracranial surgery under hypothermia in 22 cases; the data illustrated were selected from 19 cases in which detailed cerebrospinal fluid pressure measurements were made during operation. Normal cerebrospinal fluid pressure measurements (Fig. 1) were encountered in operations under hypothermia for carotid artery thrombosis and arteriovenous anomaly. Operative therapy of cerebral and pituitary neoplasms and supratentorial aneurysms permitted study of elevated cerebrospinal fluid pressure (Figs. 2 to 5).

RESULTS AND DISCUSSION

Rosomoff (1) in studies in dogs indicated that hypothermia has the following effects on the physiology of the normal nervous system: (1) decrease in cerebral blood flow; (2) corresponding reduction in cerebral

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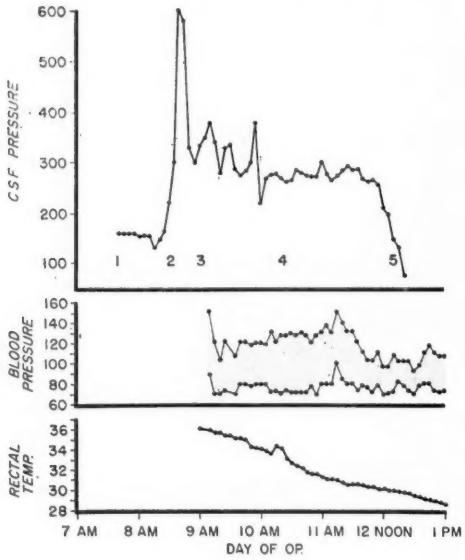
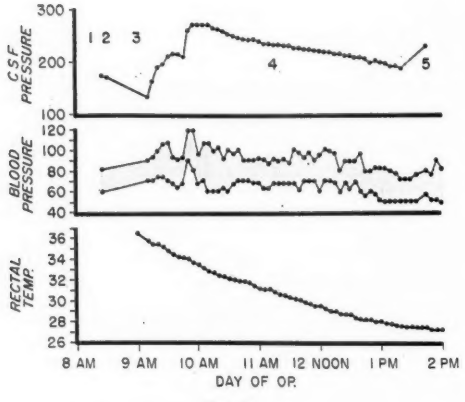


FIG. 1.



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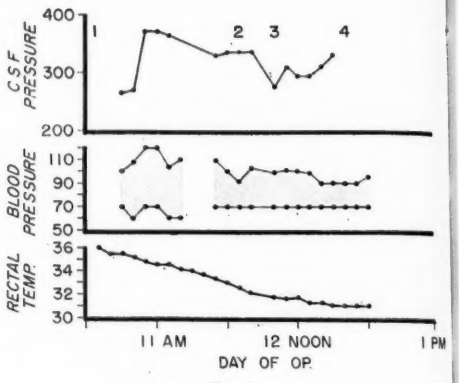

FIG. 3.

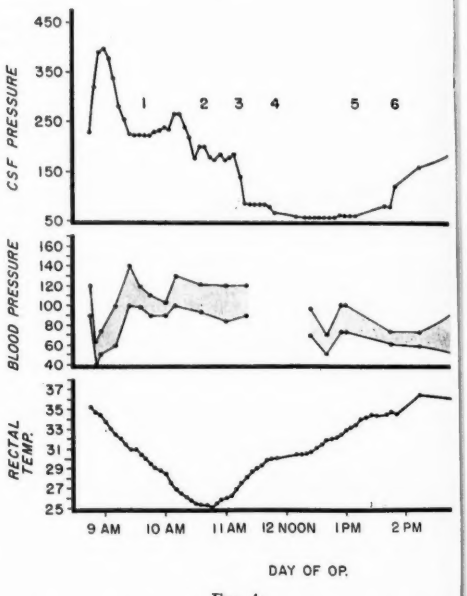

FIG. 4.

FIG. 1. Graph of rectal temperature, cerebrospinal fluid pressure, and blood pressure prior to attempted thrombectomy of intracranial portion of internal carotid artery: *1*, Tuohy catheter inserted; *2*, anesthesia and intratracheal intubation; *3*, mattress closed; *4*, scalp incision; *5*, dural opening and cerebrospinal fluid drainage. The brain filled the subdural space.

FIG. 2. Graph of rectal temperature, cerebrospinal fluid pressure, and blood pressure prior to removal of subfrontal meningioma: *1*, Tuohy catheter inserted; *2*, anesthesia and intratracheal intubation; *3*, supine in blanket; *4*, scalp incision; *5*, cerebrospinal fluid drainage. The subdural space was obliterated by the brain.

FIG. 3. Graph of rectal temperature, cerebrospinal fluid pressure, and blood pressure prior to operative therapy of a pituitary cyst: *1*, anesthesia and intratracheal intubation; *2*, scalp incision; *3*, intratracheal tube suctioned; *4*, dural opening and cerebrospinal fluid drainage. The brain filled the subdural space.

FIG. 4. Graph of rectal temperature, cerebrospinal fluid pressure, and blood pressure during operative removal of a metastatic carcinoma in the right frontal lobe (patient cooled with ice packs): *1*, scalp incision; *2*, bone flap removed; *3*, brain herniated through dural opening; *4*, hemorrhage from anterior cerebral artery; *5*, surgery completed; *6*, returned to recovery unit.

metabolism; (3) induced and compensated hypotension; (4) increase in cerebral vascular resistance; (5) decrease in brain volume; (6) diminution of intracranial and venous pressure. In the dog under normal intracranial pressure at 25 degrees C. brain volume was decreased by 4.1 per cent, and intracranial space not occupied by brain was increased by 31.8 per cent, while cerebrospinal fluid pressure and venous pressure varied proportionately with temperature during hypothermia in the studies of Rosomoff and Gilbert.

A fairly uniform pattern of increase in cerebrospinal fluid pressure was noted during intratracheal intubation and early hypothermia during the operations of these patients. Observations over a longer preanesthetic period in a patient with normal cerebrospinal fluid pressure (Fig. 1) revealed that this increase developed with induction of anesthesia. In this study operation was commenced when body temperature was reduced to 30 to 31 degrees C.; this generally afforded medium deep hypothermia at the time of dural opening. With less marked intracranial pressure or normal cerebrospinal fluid pressure, decreases in cerebrospinal fluid pressure measurements may occur (Fig. 2). This reaction is consistent with the previously cited experimental findings of decrease in cerebrospinal fluid pressure with hypothermia. This pattern, however, has not been uniform, and this variation appears related to a variety of factors, namely: depth of anesthesia, anoxia, shivering, coughing on the intratracheal tube, and possibly blood pressure. In cases in which the measurements were not appreciably reduced by the methods of the study (Figs. 3 and 4), reductions in cerebrospinal fluid pressure might have occurred had the patient been maintained in medium deep hypothermia for a longer period of time prior to dural opening. Increase in venous and cerebrospinal fluid pressure in the cooling of animals has coincided with the appearance of shivering. Figure 5 illustrates the effects of shivering during the

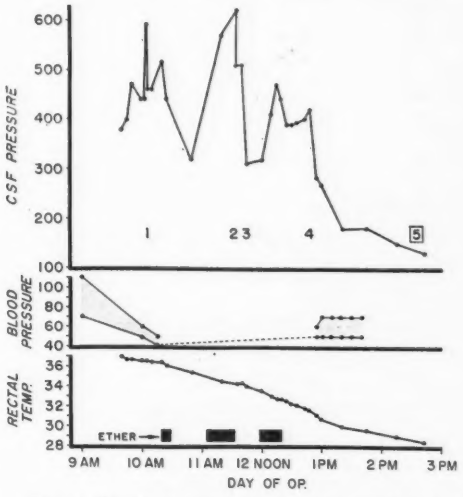

FIG. 5. Graph of rectal temperature, cerebrospinal fluid pressure, and blood pressure during temporal lobectomy for infiltrating glioblastoma multiforme (patient cooled with mattress): *1*, acute rotation of head to the left; *2*, hyperventilation with oxygen, ether having been previously administered when the patient began to shiver; *3*, skin incision and removal of bone flap followed by gradual herniation of tumor tissue and cerebral tissue through two dural defects while temperature was reduced from 34 to 31 degrees C.; *4*, dura opened widely; *5*, respiration ceased.

cooling of a patient; here an increase in depth of ether anesthesia was accompanied by a simultaneous rise in cerebrospinal fluid pressure. Although the administration of ether is known to increase intracranial pressure, the factor of anoxia was suggested in the reduction that occurred following hyperventilation with oxygen.

Observations with this method of employing hypothermia as an adjunct to surgery have not substantiated the idea that it is a practical method for reducing markedly increased intracranial pressure secondary to a space-occupying lesion. Figure 5 shows data on one of these patients who had the clinical signs, cerebrospinal fluid pressure measurements, and necropsy findings of far advanced increased intracranial pressure. Reduction in cerebrospinal fluid measurements during this operation, as in other similar types of cases of the study, correlated

with removal of the bone flap and opening of the dura; herniation of brain and tumor and increase in cerebrospinal fluid pressure occurred in this case when body temperature was being reduced to medium deep hypothermia.

No difference was apparent in the lumbar cerebrospinal fluid pressure patterns with the two methods of hypothermia employed in this study. The same pattern was seen with rapid lowering of body temperature as with slower lowering of body temperature. The usual cerebrospinal fluid pressure relationships were apparent during hypothermia. For instance, change in position from recumbency to the side resulted in the expected reduction in cerebrospinal fluid pressure, and acute rotation of the head to the side with obstruction of the venous drainage of the brain resulted in a prompt rise in cerebrospinal fluid pressure as indicated in Figure 5.

While the effect of hypothermia in reducing increased intracranial pressure has not been striking in this study, it may in many instances be accompanied by a hypotension. This is a desirable effect in intracranial surgery since it may produce a relatively bloodless operating field. Reduction in cellular metabolism and protection of cerebral tissue from hypoxia during hypotension under hypothermia appear as a responsible factor in the survival of cases in this series in which operation was complicated by massive venous or arterial hemorrhage.

SUMMARY

A study of lumbar cerebrospinal fluid pressure under two different methods of obtaining hypothermia was reported. Cerebrospinal fluid pressure measurements during intracranial operation have revealed a fairly uniform pattern of initial increase in cerebrospinal fluid pressure with induction of anesthesia and intratracheal intubation with a variety of cerebral lesions. Decrease in cerebrospinal fluid pressure was illustrated with reduction in body temperature. Variation from this pattern in other patients of this investigation appeared related to a variety of factors, namely, depth of anesthesia, anoxia, shivering, coughing on the intratracheal tube, and possibly blood pressure. The data on cerebrospinal fluid pressure during the preoperative period and evidence of herniation of tumor and brain through dural openings suggested that the methods of hypothermia employed did not afford a practical method for reducing markedly increased intracranial pressure secondary to space-occupying lesion.

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CIRCULATING LIPIDS IN EXPERIMENTAL AND HUMAN BURNS

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ON THE BASIS of isolated observations on the role of lipids in inflammation and hemolysis, a study of the effect of thermal injury on tissue and circulating lipids was begun. In previous reports the initial findings of this work were noted. In experimental burns in the dog, pig, and rat, lipids were found to leave the burned area and appear in large volumes in the lymph draining the burned area. These lipid shifts were acute and largely of lipid phosphorus, cholesterol, and glycerol. There was a gross outflow both in actual quantity and in concentration of these lipid constituents in the lymph (2, 3). This study was continued in order to try to assess further the lipid changes and to determine their significance in the clinical picture of the burned patient.

The study was continued by posing four questions: (1) What was the duration and further make-up of the lipid shift in the experimental burn, and the source of this mobilized fat? (2) Was this lipid noxious in any way to the organism? (3) Was this lipid in the microscopic particle size or was it largely molecular? (4) Were these lipid shifts detectable in the human and, if so, in what form?

These questions will be discussed in order:

1. The experimental procedure for collection and analysis of lymph draining from the burned foot of a dog was the same as described previously (2). The lymph so obtained was analyzed for total lipid, lipid phosphorus, cholesterol, glycerol, and fat acids. It was further studied by paper electrophoresis by using minute aliquots and staining the paper with bromphenol blue and oil red O.

The results of this study are shown graphically in an average of 15 animals in Figures 1 to 5. All of the lipid constituents followed the same curve. There was a marked initial rise which then dropped slowly over the next 4 days. Normal lymph lipid levels were not reached until the burn was healed.

In previous work using histochemical techniques, phospholipid was found to leave the burned dermis. This work was done on a qualitative basis on biopsy material; however, it did not account for the large amount of lipid found in the lymph draining from the burned area. An attempt was made to trace the lipid phosphorus from the blood stream, through the burned area. To do this, a donor dog was infused with radiophosphorus. Twenty-four, 48, and 72 hours later blood was withdrawn and found to have radioactive lipid phosphorus. The 24 hour sample had the highest radioactivity. Blood was withdrawn from the donor dog at this period, infused into a recipient dog and allowed to equilibrate. Then one foot of the dog was immersed in water of 70 degrees C. for 1 minute and lymph was collected from the burned foot and a normal foot. Counts were made on these lymph samples as well as on samples of venous blood draining the foot. Parallel lipid determinations were done as well. There was no difference in the venous plasma count between the two legs. There was a great increase in the total (both organic and inorganic) radioactive phosphorus in the lymph draining from the burned foot (Table I).

Further examination of the lipid mobilized

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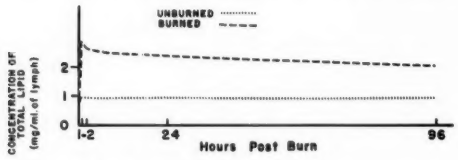

FIG. 1. Average total lipid concentration.

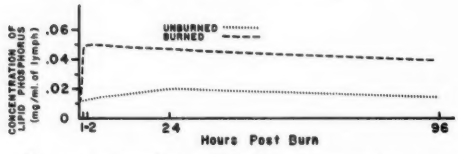

FIG. 2. Average lipid phosphorus concentration.

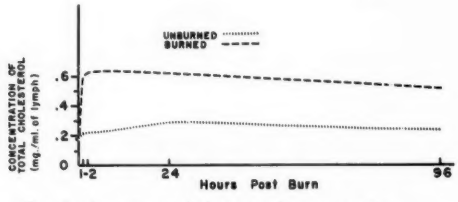

FIG. 3. Average total cholesterol concentration.

FIGS. 1 to 3. The average total lipid, lipid phosphorus, and total cholesterol concentrations in lymph draining from a burned dog extremity go up immediately and remain elevated for more than 4 days.

by the burn was done to ascertain its relationship to proteins. Using paper electrophoresis by the method of Block, Durrum, and Zweig, patterns were developed before and after burn of both the unburned and burned foot of the dog.

A series of 10 dogs with a total of 30 samples were run (Fig. 6). Dog 18 is a representative animal. Five curves are shown in this graph.

It can be seen that the preburn and postburn control samples follow the same curve. The burn samples (*B* and *C*) show a marked increase in lipoprotein. The rather high levels of lipoprotein in the lymph after the burn confirmed the observations made by chemical and isotopic analysis.

2. Two approaches were made to the problem as to whether the lipid isolated from an experimental burn was noxious in any way to the organism. It had been postulated in previous discussions of the role of lipids in burns that the lipid might be a hemolytic substance. To test this hypothesis, lymph was collected from the legs of dogs in the course of the experiments outlined. One foot was immersed in water of 70 degrees C. for 1 minute. Lymph samples were collected at varying intervals from 15 minutes to 5 days following the burn. These were mixed with the blood collected prior to the burn and incubated for 2 hours. A portion of this was mixed with Simmel's solution of 35, 45, 65, and 75 per cent. Following centrifugation, hemoglobin from hemolyzed erythrocytes was quantitated by the spectrophotometer.

There was no consistent difference between the red cell fragility when red blood cells were incubated with lymph from the burned as compared to the unburned extremity; there was no alteration of red cell fragility by incubation with lymph collected at different periods after burn, either.

Figure 7 represents a graphic compilation of results averaged from 15 dogs plotted on a semilogarithmic scale. The apparent fragility of red cells mixed with the lymph collected during the 2 hours after the burn has not been reproduced by 6 subsequent experiments focused on this period. This technique does not indicate any consistently demonstrable hemolytic agent in the lymph from a burned extremity.

Despite the fact that many previous studies have failed to demonstrate a circulating toxic substance after a burn, it was decided

TABLE I.—RADIOACTIVE PHOSPHORUS COUNTS IN LYMPH DRAINING FROM BURNED AND UNBURNED EXTREMITIES

	Immediate post burn	*1 hour post burn*	*2 hours post burn*
Burned leg			
Inorganic P_{32} + organic P_{32} dis./min./ml.	—	128	111
Tagged lipid phosphorus dis./min./ml.	—	67	63
Percentage of tagged lipid phosphorus in the combined counts		52	56
Unburned legs			
Inorganic P_{32} — organic P_{32} dis./min./ml.	—	26	23
Tagged lipid phosphorus dis./min./ml.	—	7	9
Percentage of tagged lipid phosphorus in the combined counts		27	39

at least to test the lipoprotein component of plasma by a series of simple experiments. Nine young Chester white pigs of 10 to 15 kilograms were given a 30 per cent burn by immersion of the back and flanks into water of 70 degrees C. for 1 minute. Blood was drawn from the superior vena cava before and after the burn at 2, 24, 48, 72, and 96 hour intervals.

The plasma was extracted, ultracentrifuged at different specific gravities at 105,000 G. This supernate was withdrawn and injected intravenously into mice. At no specific gravity was there any effect demonstrated in the mice (Table II).

3. Using the technique described by Pelthier, plasma from a series of burned animals and patients was studied to determine whether this lipid was in the microscopic particle size or largely molecular. Two to 3 milliliters of heparinized plasma were stained with phosphin 3R, and droplets were examined under an ordinary microscope by using ultraviolet light. Particles of fat were found in the plasma of a few pigs and 2 patients (Table III).

These observations suggest that fat emboli of microscopic size are not uncommon in the blood stream after a burn. The number of samples examined was small, however. Most of the circulating lipid must be in molecular size.

4. Fourteen burned patients of all ages and with varying types of burn were examined to determine whether lipid shifts were detectable in the human and, if so, in what form. However, because of complicating disease, multiple transfusions of plasma and blood during the study period, and complicating surgical treatment, only 11 patients and a few more control patients were studied for circulating lipids.

TABLE II.—LIPOPROTEIN TOXICITY STUDIES OF PLASMA FROM BURNED PIGS

Plasma Sp. g.	*No. of pigs*	*No. of centrifugations at 105,000 G*	*Result in mice*
1.006	2	3	No effect
1.019	3	2	No effect
1.073	2	1	No effect
1.178	2	0	No effect

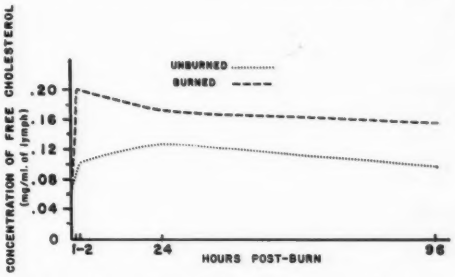

FIG. 4. Average free cholesterol concentration.

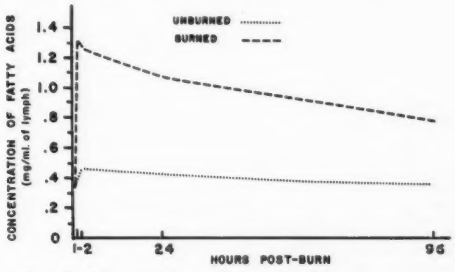

FIG. 5. Average fatty acid concentration.

FIGS. 4 and 5. The average free cholesterol and fatty acid concentrations in the lymph draining from a burned extremity show an even more striking rise after a burn than the other constituents.

Blood was collected in heparinized tubes from the patient as soon after the burn as possible; then at 24, 48, 72 hours, and 1 week. The plasma so obtained was examined by previously described techniques for total lipid, cholesterol, lipid phosphorus, and fatty acids. Some was studied for particle size lipids and by electrophoresis.

Over 300 determinations of plasma lipid components were made; however, the 2 patients plotted in Figure 8 are examples of the

TABLE III.—LIPID PARTICLES DEMONSTRATED IN PLASMA OF BURNED PATIENTS AND EXPERIMENTAL ANIMALS

Origin of plasma	*Time of sample*	*Lipid particles observed*
Patient with hiatus hernia	2 hrs. postoperative	Particles of 25_M in diameter
12 per cent burn in 21 mo. old child	24 and 48 hrs. after burn	One small particle seen in 48 hour sample
Pig 1, 30 per cent burn	2 hrs. after burn	Particles of 100_M diameter
	48 hrs. after burn	Particles of 20_M diameter
Pig 9, 30 per cent burn	2 hrs. after burn	Particles of 24_M diameter

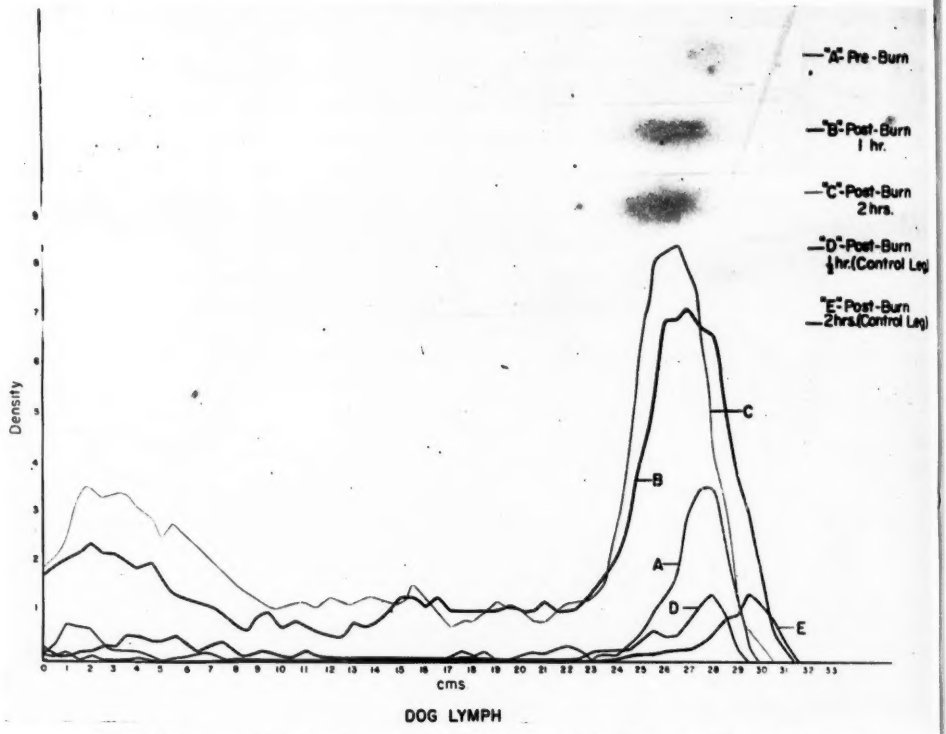

FIG. 6. The paper electrophoretic patterns are at the top of the illustration. The graphs represent the densitometric readings of these patterns. Curves *A*, *D*, and *E* are the control lipoprotein readings. Curves *B* and *C* are the postburn lymph lipoprotein readings.

group and represent nearly average figures. It will be noted that none of the determinations fell above or below the normal range of the controls. There were no truly suggestive trends which could be determined from these figures. It is interesting that all of the lipid components dropped precipitously immediately prior to death in the 1 patient of the series who died. Another patient who remained critically ill for some weeks but finally recovered had a less marked drop in all plasma lipid constituents.

TABLE IV.—BURN PATIENT SERIES

Patient No.	*Age*	*Per cent of burn*	*Degree of burn*	*Grafted*	*Blood or plasma Rx*	*Remarks*
1	31	10–12	3	Yes	Yes	Epileptic
2	72	12	3	No	No	Ca lung
3	34	9	3	Yes	Yes	
4	31	15	3	No	No	Died
5	1½	7	1 & 2	No	No	
6	4½	65	3	Yes	Yes	
7	3	2	1 & 2	No	No	
8	34	15	2	No	No	
9	20	10	2	No	No	
10	20	12	2	No	No	
11	23	5	1	No	No	
12	20	15	1 & 2	No	No	
13	9	8	1 & 3	Yes	No	
14	64	5	3	Yes	No	Diabetic

Using paper electrophoresis as an indicating medium, an attempt was made to establish a definite pattern analysis in the lipoprotein-lipid fraction and albumin-globulin fraction of varying circulatory fluids subjected to moderate thermal injury.

A series of 9 controls was used to establish a reference pattern for the lipoprotein and lipid fractions in the plasma. The subjects used were hospitalized patients with minor disorders; for example, hernia. Eleven burned

patients were studied whose ages ranged from 17 months to 72 years. The intensity of the burns varied from 2 to 15 per cent of the body surface, with the exception of 1 patient with a 65 per cent burn. Thirty-six samples were run varying from 2 hours to 21 days after the burn.

Optical density readings of the stained paper electrophoretic patterns were plotted against centimeters of migration on each sample of plasma. A lower set of values was established by the denser areas in the scattergram than that of the reference pattern from the control series. Average results are shown in Table V.

The immediate postburn alpha fraction appeared to be in the normal range, taking a drop in the 24, 48 hour, and 7 day postburn samples, then rising to normal in the 14 and 21 day samples. Little change was noted in the beta fraction of the lipoprotein and lipid curves.

Case 7 was representative of 10 of the 11 cases studied. The samples of blood in this case range from 2, 24, 48, and 72 hours, 7 and 14 days after burning. The patient, a 39 month old white male child, pulled a bowl of hot cereal over himself, resulting in a first and second degree burn covering 3 per cent of the body area. No treatment had been given prior to the collection of the first blood sample. The course of the lipoprotein and lipid fractions followed closely the course taken by the averages curves illustrated in Figure 9.

Here, a steady alpha level was maintained up to the seventh day after burn, then at the fourteenth day an increase was observed. The beta fraction showed a higher value in this case than the average, but no significant change was noted in the over-all picture.

The paper electrophoretic patterns of plasma from a series of 10 pigs, burned over 30 per cent of the body surface were studied. The lipoprotein and lipid curves were plotted on scattergrams and average curves drawn. Samples consisting of control, 2, 48, 72, and 96 hours postburn samples were taken. Average results of the photometer reading were computed. No change from the normal curve was noted.

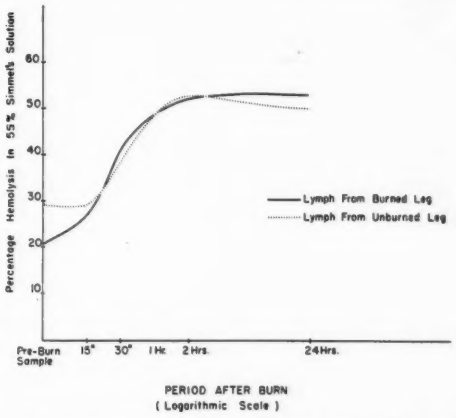

FIG. 7. Graphic compilation of the hemolytic effect of lymph draining from a burned foot shows no greater hemolysis than was produced by lymph from a normal foot.

DISCUSSION

It has been established that in the experimental burn, lipid is mobilized from the burned area and through the vascular bed in the burned area into the lymph draining from this area. Other laboratories have found increased circulating lipids in one form or another in the plasma of burned animals. There are suggestions of such changes in the burned patient, though study of the untreated burn must necessarily be of minor burns, as major ones must be treated, thus obscuring gross circulating lipid changes. Despite these difficulties, observations of significant lipid shifts in burns, trauma, and irradiation injury are being made.

TABLE V.—AVERAGE RESULTS OF LIPOPROTEIN AND LIPID FRACTIONS IN BURN PATIENTS

	Centimeters of migration							
	Alpha fraction				*Beta fraction*			
Time post	*Optical density readings*							*No. of*
burn	*2*	*6*	*10*	*14*	*18*	*22*	*26*	*samples*
2–5 hrs.	39	50	25	12	16	14	05	2
24 hrs.	20	31	15	9	15	18	5	5
48 hrs.	37	36	19	16	22	17	7	7
7 days	29	34	17	14	15	12	8	8
14 days	48	56	17	21	20	11	0	8
21 days	54	65	25	21	31	14	0	2

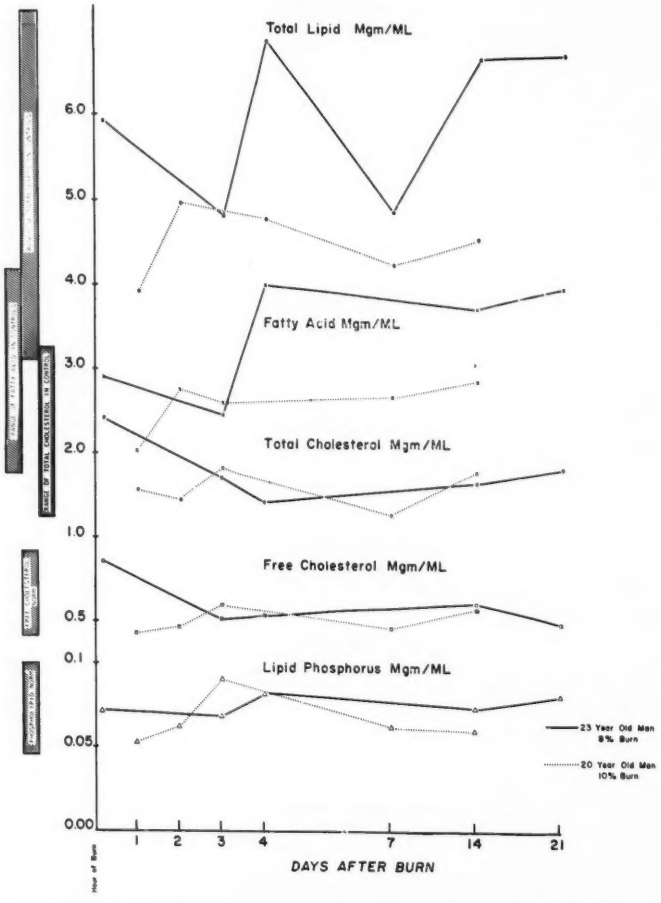

FIG. 8. Lipid components in the circulating plasma of burned patients show no variation out of the normal range, at least, as indicated in these 2 untreated burns.

What role, if any, this lipid may play is unknown. No detrimental effect has been demonstrated in this work or in the work of others. Whether the final effects are not realized for some time has not been determined. It has been suggested by Pollak that the eventual effects of lipid mobilized by trauma, thermal injury, or irradiation may be reflected by an increase in atherosclerosis. Further observations will be required to confirm this theory.

The manner in which lipid is mobilized after thermal injury may be significant as well. Apparently it is largely in the molecular and protein bound form. Whether the integrity of the protein linkage is preserved may be a significant factor in the role of these lipids. The alteration of the proportion of alpha and beta lipoprotein in the patient who died of his burns suggests that this reaction is associated with a poor prognosis.

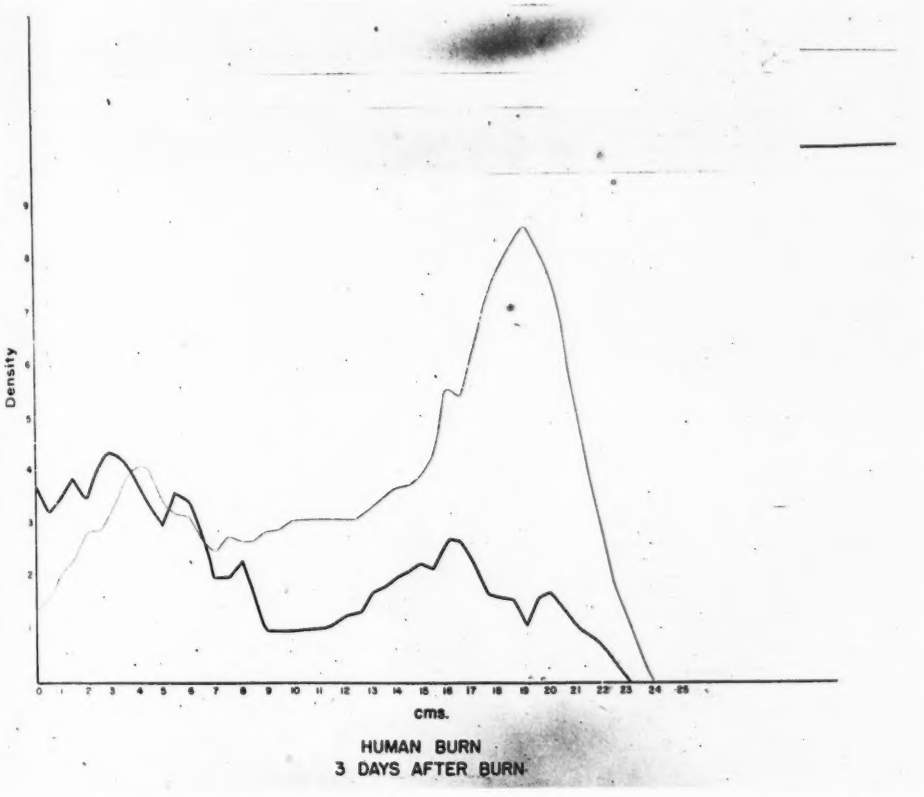

FIG. 9. By comparing the dark line (lipoprotein densitometry pattern) in this 3 year old burned child, it is apparent that no gross deviation from the average curve has occurred.

SUMMARY AND CONCLUSIONS

In a previous report it was noted that rather large amounts of lipid were mobilized from an experimental burn into the lymph draining the area. The study was continued to determine the source, further make-up, and extent of this circulating lipid, as well as any possible effect it might have.

By using radioactive phosphorus tagged lipid, it was demonstrated that a large proportion of lipid went through the burn from blood circulating through the area. It was further found that the lipid flow from and through the burn persisted for a longer period than other constituents such as protein and electrolytes. The chief form of this lipid seemed to be in the lipoprotein fraction and was largely one of a reversal of the normal alpha and beta components. This was found to be true in lymph and blood in experimental burns, and in plasma in human burns.

Attempts to demonstrate a hemolytic or toxic effect of these lipid shifts were unsuccessful. The lipid may be present in a microscopic particle size, but was found to be present largely in the molecular form and there is some doubt that fat emboli play any great role.

Examination of the circulating plasma of human burned patients showed few certain changes, possibly because all of these pa-

tients had been treated with blood plasma or with surgical excision. A definite drop in the total lipid and in other constituents was associated with a poor prognosis in 2 instances.

The observations in both experimental and clinical burns suggest that this reaction of lipids is a unique one, making the acute burn, in this respect at least, quite different from a surgical wound.

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THE ROLE OF WATER SOLUBLE CONTRAST MEDIA IN GASTROINTESTINAL TRACT OBSTRUCTION

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FEAR OF COMPLICATION in an intrinsically dangerous situation has virtually prohibited the use of conventional opaque contrast media in cases of suspected or apparent intestinal obstruction. Despite the obvious desirability of delineating lesions involving the gastrointestinal tract, the hazards of impacted barium and peritoneal spillage during surgery and inspissated barium in the postoperative period almost entirely interdicts its use.

Before the judicious application of an opaque contrast media can be recommended for diagnostic radiography in an acute condition of the abdomen these primary objections must be obviated and the following criteria satisfied: (1) The media must provide diagnostic contrast for fluoroscopic and radiographic examinations. (2) The media must not be difficult to administer to debilitated and critically ill patients. (3) Intrinsic toxicity of the media should be absent or negligible under a wide range of circumstances. (4) Administration of the media must not, in any manner, add to the existing pathologic condition by local irritation or by subsequent mechanical impaction or inspissation. (5) The media must not interfere with surgical efforts to correct the causative lesion at any time after the radiographic examinations. (6) Excretion of the media must, preferably, be independent of the gastrointestinal tract.

It is our purpose in this article to review the clinical application of a compound which best approximates the requirements outlined. The study was conducted over a 9 month period and includes an unselected total of 50 patients who presented the problem of intestinal obstruction as a surgical emergency. Each of these patients was examined with a solution of water soluble hypaque sodium administered either by mouth or by enema. In no instance was the concentration of the solutions employed greater than 20 per cent and, in most cases, was no more than 10 per cent.

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BACKGROUND

Previous studies with diatrizoate sodium hypaque have referred almost exclusively to its use as a media for urography. Few and minimal side reactions in addition to satisfactory delineation of the renal collecting systems have characterized its use. Our continued experience (2) with this media in urography has extended well over a thousand cases, and in no instance has iodinism been associated with its application. The pharmacology of the compound has been adequately described elsewhere (3). Efforts to utilize thorotrast, lipiodol, and iodochlorol in the gastrointestinal tract antedate the present study and testify to the tenacious resistance this problem has had to solution. Thorotrast presented the complication of residual radioactivity in addition to the high viscosity, unpalatability, and difficulty in administration that it held in common with the other oily substances.

Canada has reported on the use of water soluble urokon in 13 patients, with solutions ranging in strength from 15 to 70 per cent with particular success in the evaluation of colitis and defunctionalized colons.

MATERIAL AND RESULTS

Hypaque sodium was obtained in powdered form in 25 gram vials. Its use was con-

FIG. 1. A single glass (12 oz.) of 15 per cent water solution of hypaque showed this massive lesion of the antrum in a 64 year old female who presented with a palpable, epigastric mass and equivocal signs of gastric obstruction. Site of the partially obstructing lesion is seen. Further studies allowed a more thorough definition of the nature of the lesion which was proved a primary gastric carcinoma at surgery. Use of hypaque offered a rapid means for dealing with an equivocal but serious clinical problem without compromising patient's welfare.

FIG. 2. In this case a 10 per cent water solution of hypaque was taken orally to evaluate the presence of tumor recurrence and constriction at the site of a choledochal jejunostomy done 1 year previously. No untoward after effects resulted from the retrograde passage of the hypaque, as can be observed on the film, into the hepatic radicles. With the elimination of the presence of an obstruction, detailed studies were conducted with much greater assurance in order to evaluate the site of the anastomosis.

fined to adult patients in whom the use of barium was feared by the referring physician. The diagnostic categories included 6 cases of gastric obstruction by cancer or benign ulcer, 12 cases of diverticulitis, 1 case of volvulus of the sigmoid colon, and 1 case of a common bile duct-jejunal anastomosis. Small bowel obstruction, colitis, and large bowel cancer comprised the remainder of the groups. In 15 of the 50 cases, surgery followed within 24 hours of the administration of the water soluble contrast solution.

Use of the water soluble contrast media to demonstrate mass lesions involving the upper gastrointestinal tract is shown in Figures 1 and 3.

The hypaque solution was given orally in 21 patients. It was particularly satisfying to find that carbonated soda water or plain water could be used as a vehicle to dissolve the powder and form a solution which was never unpleasant to taste. The addition of flavoring compounds caused no interference. The concentrations of the solutions were varied from 10 to 20 per cent. Within this range, diagnostic radiography could be achieved with slight differences in quality dependent upon the patient's body habitus. A single 8 ounce glass was usually sufficient to provide films of gross diagnostic quality. Additional quantities could be used without difficulty and total quantities of 100 grams of powder were given without untoward reaction.

Though careful follow-up films were taken at hourly intervals and at 6, 12, 24, and 48 hour periods whenever possible, a clear-cut pattern of absorption of the hypaque from the gastrointestinal tract was not established. In only 1 case of small bowel

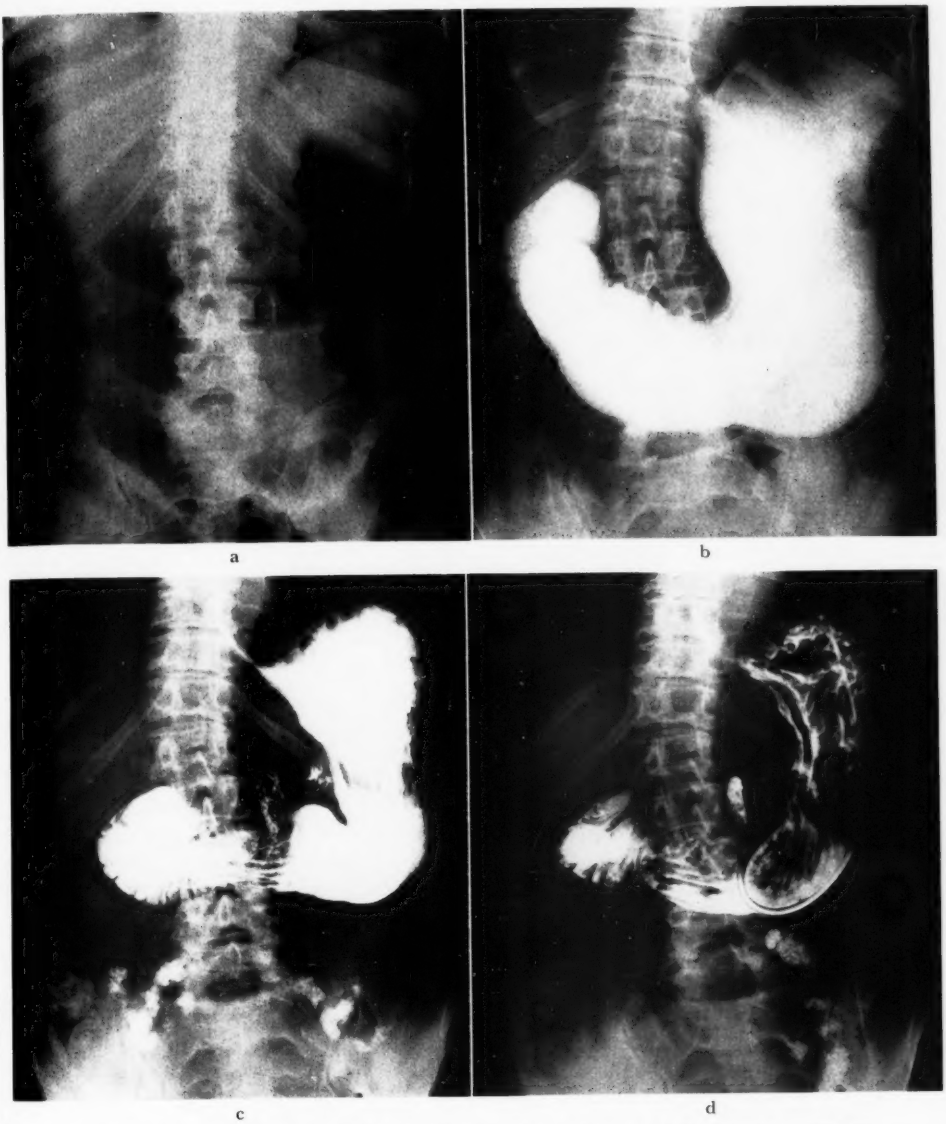
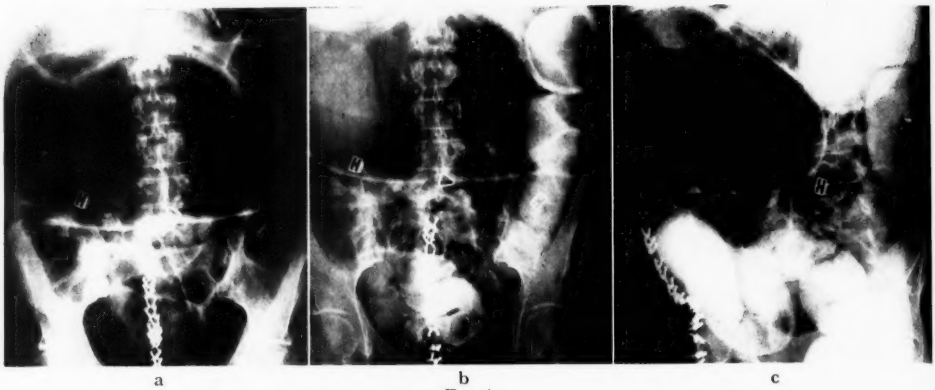
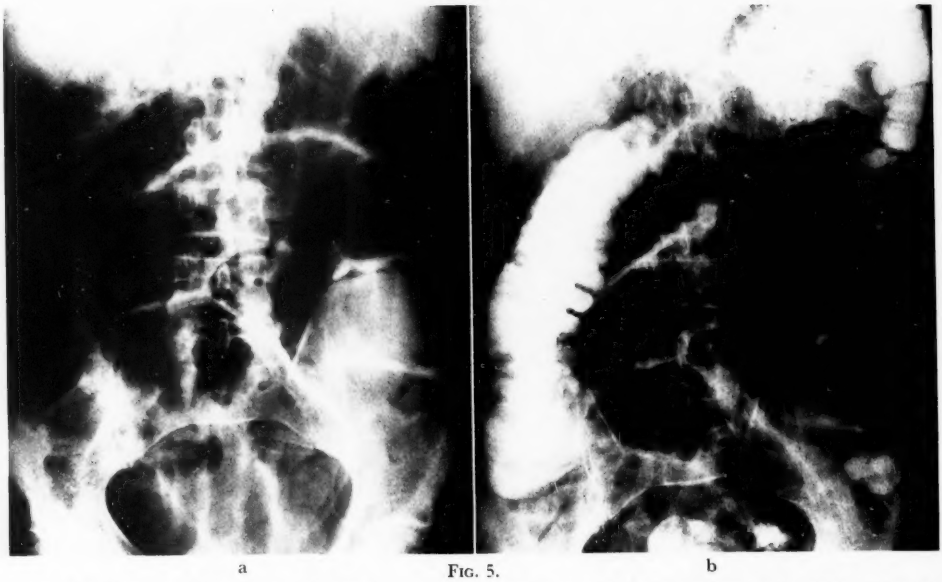


FIG. 3. a, The plain film of the abdomen shows moderate distention of the stomach, separation of distended small bowel loops, and probable ascites in a 71 year old woman hospitalized because of weight loss, signs of intermittent high obstruction, and a large, palpable epigastric mass. b, After the oral administration of a 12 ounce glass of 10 per cent water solution of hypaque, no contrast media could be observed beyond the duodenal-jejunal junction. c and d, A gastric tube was introduced then and the fluid contrast media was removed easily. With this maneuver, the site of a constricting carcinoma at the duodenal jejunal flexure was outlined. A small portion of the contrast media had passed through the area of partial obstruction by this time. A very satisfactory mucosal pattern was also obtained.



a b c

FIG. 4.



a b

FIG. 5.

FIG. 4. a, The plain film of the abdomen shows massive distention of segments of large bowel in a 41 year old woman examined 8 days after cesarean section with clinical findings of progressive abdominal cramps and distention. The transverse diameter of the cecum measured 13.5 centimeters. Though volvulus of the cecum was suspected from the plain film, a lesion at the colonosigmoid junction could not be excluded entirely. b and c, An enema of 10 per cent hypaque water solution was given cautiously and indicated the absence of a lesion in the sigmoid or descending colon. Exploration within 2 hours of the enema revealed a volvulus of the cecum. The hypaque produced no untoward effect prior, during, or after the surgical procedure.

FIG. 5. A 70 year old male hospitalized because of weight loss, anorexia, and nausea associated with a fixed, large left lower quadrant mass which had not altered his bowel habits. a, Poorly defined, distended loops of bowel on the plain film did not allow for delineation of the mass or answer satisfactorily whether a presumed obstruction was actually present. b, The rectal administration of a 15 per cent water solution of hypaque disclosed the contrast media to flow throughout the large bowel without evidence of an intrinsic lesion. Persistence of an extrinsic pressure defect, however, along the mesial aspect of the descending colon was interpreted as secondary to a retroperitoneal tumor. At operation, a nonresectable, retroperitoneal, anaplastic sarcoma was found. In this instance the hypaque provided a means for distinguishing large from small bowel without danger of subsequent obstruction due to inspissation, had an obstructing lesion been present as feared clinically.

obstruction could residual hypaque be demonstrated at the end of 72 hours, and in this case it produced no difficulty. Its disappearance was noted most often between 24 and 48 hours after its administration. In a patient with obstruction at the pylorus secondary to gastric cancer, a film of the abdomen, 12 hours after surgery and 24 hours after the use of hypaque solution, revealed the opaque material distributed in the large bowel. The surgeon did not observe contrast media during his operative procedure. The fluid material in the bowel, moreover, offered no deterrent to the surgery.

Except for the case in which there had been surgical anastomosis of the common bile duct and the jejunum, no contrast media was ever visualized in the hepatic or biliary system. No cholangitis was noted subsequent to its use (Fig. 2).

In none of the 50 patients could evidence on a pyelogram be distinguished.

The administration of water soluble contrast solutions, varying in strength from 12 to 20 per cent, by means of an enema provided equally satisfactory results in studies of the large bowel. No exacerbation of diverticulitis was observed (Figs. 4, 5, and 6).

Identification of distended bowel loops, often difficult in young patients, presented no problem with the use of this media. Distinction between large and small bowel could be obtained without delay and with relative ease.

The appraisal of stenotic lesions of the large bowel, in which immediate surgical relief is required, formed the bulk of the cases evaluated and offered the best demonstration of the utility of water soluble contrast media. The absence of surgical complications secondary to its use and the elimination of any danger of impaction have promoted the free use of this compound in delineating lesions of the large bowel.

Neither the oral nor the rectal route resulted in any evidence of iodinism during the entire study. This condition was considered carefully because of its theoretic potential as a hazard.

FIG. 6. A 72 year old woman admitted with signs of large bowel obstruction and a tender right lower quadrant mass was examined with a 12 per cent water solution of hypaque introduced per rectum. The demonstration above of an annular, obstructing cancer was confirmed at operation 24 hours later. The residual hypaque presented no surgical difficulty and did not produce any subsequent peritoneal reaction.

Reports from the surgeons revealed that no contrast material could be seen or felt during the surgical procedure. The apparent absence of peritoneal irritation following the use of the contrast medium was another source of satisfaction.

In the 20 patients in whom no obstruction could be demonstrated, with diatrizoate sodium solution, the subsequent use of barium was undertaken with free assurance to elucidate the diagnosis.

The use of a 10 per cent solution of this material to exclude the presence of a suspected pyloric obstruction in a 5 week old infant provided an excellent diagnostic evaluation without any untoward effects.

We do not believe that water soluble contrast media can substitute for barium in the delineation of mucosal pattern. It is a very satisfactory means for the demonstration of

the gross appearance of a lesion when barium cannot be used. It is impressive to note the complete absence of side reactions in the patients who, for the most part, were dehydrated, debilitated, and acutely ill.

As a result, within our department, there has been no hesitation to the use of hypaque powder solution in the study of acute conditions of the abdomen. This procedure has allowed the referring physician to delineate his program of action with increased confidence. It is within this sphere of use that water soluble hypaque powder achieves a significant contribution in the study of the gastrointestinal tract.

SUMMARY

Water soluble contrast media offers the radiologist, who is confronted with the problem of an acute, surgical abdomen, a diagnostic, radiographic media which is free of apparent toxicity, easy to use, and satisfying to the surgeon in its absolute freedom from inspissation or impaction. Judiciously used water soluble hypaque appears to present the method of choice in the radiographic evaluation of gastrointestinal obstruction when the use of conventional media is contraindicated.

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PAROTIDECTOMY FOR CHRONIC OR RECURRENT SIALADENITIS

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IN THE TREATMENT of chronic or recurrent parotitis, surgical removal of the diseased gland has been almost universally avoided according to Eddey and McKenzie. The fear of injury to the facial nerve or its branches has been the prime deterrent. In 1935, Dorrance cited the danger of dividing the facial nerve, the danger of fistula formation postoperatively, and the price in time and suffering to the patient as militating against making surgical removal a satisfactory procedure. In 1942, Beck stated: "Excision of the parotid gland is a formidable procedure and is practically never done except for malignant growths." Gerry and Seigman, in 1955, wrote: ". . . in general, excision of the parotid gland is not surgically feasible in the management of chronic parotid sialadenitis." If surgeons have thought that the hazard of injury to the facial nerve has been sufficient to warrant enucleation of the potentially dangerous mixed tumor in preference to parotidectomy, then this reluctance toward the performance of parotidectomy for the benign condition of parotitis is consistent.

Rather than parotidectomy, the treatment of chronic or recurrent parotitis has involved the employment of various agents and procedures, including radium and roentgen therapy as mentioned by Adner and Dorrance; dilatation of Stensen's duct by probes and by liquids, as in the performance of sialography reported by Hobbs and Sneierson and by Pyrah; removal of septic foci, such as teeth and tonsils; agents to decrease the viscosity of salivary excretion, such as potassium iodide and pilocarpine; massage; oral hygiene; autogenous vaccines; and, more recently, antibiotic therapy. The effectiveness of these conservative approaches to the problem must be viewed in the light of several factors. At the outset it should be recognized that the fact that no single method has been clearly demonstrated to be superior to the others tends to make all of these approaches suspect.

The protean nature of chronic or recurrent parotitis makes evaluation of a given method of therapy extremely difficult. We are not herein considering other types of inflammation of the parotid gland, such as epidemic, postoperative, or acute suppurative parotitis. Rather, we are considering that type of inflammation well described by Bigler and Payne in which there are persistent or recurrent bouts of swelling and pain in one or both parotid glands. It is generally believed that initially the infection is an ascending one via Stensen's duct. Many believe that the inflammation is secondary to an inflammation or abnormality about the teeth or elsewhere in the mouth. Often various organisms, most frequently Streptococcus viridans, can be cultured from the duct. Although only a small percentage of calculi of the salivary glands occur in the ducts of the parotid gland, calculi can be the causative factor of chronic parotitis. Occasionally, one may see a patient with multiple small calculi scattered throughout the parenchyma of the gland. If these patients are experiencing repeated bouts of pain and swelling, with low grade fever, they are candidates for parotidectomy. On the other hand, a patient may be

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a b

FIG. 1. Case 5. Chronic recurrent parotitis involving both parotid glands for which bilateral (superficial right, total left) simultaneous parotidectomy was carried out. a, Preoperative appearance. b, Appearance 1 week postoperatively. Slight weakness of the right marginalis branch of the facial nerve was present for 2 weeks.

seen with a single stone in the duct for which only simple extraction is necessary. As the condition of chronic parotitis progresses, in all probability some obstruction from the inflammatory process is a factor in progression of the disease.

Patients with chronic or recurrent parotitis, untreated or treated conservatively, vary greatly from the standpoint of frequency, duration, and severity of the bouts. Some patients have a single mild episode, a day or two in duration. Commonly, a patient will have a bout of pain and swelling of the parotid gland that persists for several days or weeks. The symptoms may recur once or twice in the same or opposite gland at intervals of weeks or months, never to return again. Others have frequently recurring to constant severe trouble for a period of years. This can occur whether or not the patient has received any or several of the various treatments ordinarily used. It is in this group of patients that we believe that superficial or total conservative (nerve preserved) parotidectomy is indicated.

Table I lists data on 5 patients with chronic or recurrent parotitis treated by superficial or total conservative parotidectomy during the past 18 months. All 5 were sufficiently distressed by their trouble to be exceedingly anxious to be rid of it. One patient had equal involvement of both parotid glands (Fig. 1). Three patients had had constant or recurring trouble for a period of 9 years or more. One patient had had constant trouble for 1 year. One patient had had massage and roentgen therapy, 2 patients had received massage and vaccine,

TABLE I.—DATA ON 5 PATIENTS TREATED FOR CHRONIC SIALADENITIS

Case No.	Age and sex	Symptoms and duration	Previous treatment	Surgery	Comment	Pathology	Result
1	45 F	Recurrent pain and swelling of r. parotid often with colds and ear infection. Thick mucus from Stensen's duct. Str. viridans cultured. (5 yrs.)	Massage, vaccine	Total conservative parotidectomy 10-25-55	Dilated ducts. Stone in Stensen's duct	Chronic sialadenitis. Sialolithiasis	Excellent (temporary paresis of facial nerve —4 wks.)
2	54 M	Swelling and discomfort of l. parotid with each meal. Thick mucilaginous saliva. Str. viridans cultured. (9 yrs.)	Massage, vaccine	Superficial parotidectomy 12-15-55	—	Cystic changes and fibrosis	Excellent
3	51 M	Swelling and pain of r. parotid. Roentgenogram: small calcific areas in gland. (9 yrs.)	None	Superficial parotidectomy 2-11-56	Marked cystic enlargement of parotid duct	Cystic dilatation of ducts with marked inflammatory response	Excellent
4	46 M	Swelling of r. parotid at mealtime. Spontaneous remission after meals. (1 yr.)	Massage, x-ray	Superficial parotidectomy 2-16-56	Obstruction of duct as it projected deep into masseter muscle	Chronic sialadenitis	Excellent
5	46 M	Pain and swelling in both parotids. strep. and staph. cultured. (11 yrs.)	Massage, chloramphenicol	R. superficial parotidectomy, l. total conservative parotidectomy 3-28-57	Cystic dilatation of ducts and dense fibrosis of parenchyma	Focal obliteration of lumen of Stensen's duct on left. Fibrosis and infiltration on right	Excellent (slight paralysis on right—1 wk.)

and 1 patient, massage and chloramphenicol (chloromycetin). In 3 cases Streptococcus viridans was cultured from Stensen's duct. In all 5 cases obstruction was thought to be present, in 1 by a stone in Stensen's duct, and in 4 by inflammatory swelling. Subsequently, in all 5 cases, the histologic examination of the excised gland showed cystic and fibrotic changes from inflammation. These patients have all received excellent results from the surgical treatment and have remained completely free of symptoms since the operation.

Criteria for the selection of patients for surgical treatment are not clear-cut. Operation is not recommended for all patients with recurrent parotitis, as many or most will have but one or a few mild episodes, followed by no further trouble. The indications must be based on the clinical picture, namely, the distress caused the patient by the disease, the frequency of attacks, and the duration of the trouble. In the 5 cases presented, we believed that the disease had progressed to the extent that there were irreversible changes in the gland, with the resultant element of obstruction, and that hope for spontaneous or medically induced remission did not exist. The pathologic findings in each of the 5 cases seem to have borne this out.

Sialography was not utilized as an aid in the selection of patients for operation. If the nature of the patient's symptoms qualified him for parotidectomy, the absence of confirming signs by sialography would not affect the qualifications. Conversely, if the nature of the patient's symptoms were such that he was not believed to be a candidate for operation, any evidence by sialography of sialadenitis would not make him a candidate.

Some patients present a localized mass in the parotid gland which clinically cannot be differentiated from a neoplasm. These patients should be given the benefit of exploration, or at least of needle biopsy, even though sialography should show changes in the ducts suggestive of sialadenitis. Sialography can outline the ductal system well but, unfortunately, it cannot effect visualization of the parenchyma of the gland.

Tumor or sialadenitis can be present with or without sialographic evidence of it as

shown by Rose. Any localized mass in the parotid gland should be treated as a neoplasm until its pathologic nature is known, and any sialadenitis, because of its benign nature, should be treated surgically only on the basis of the clinical picture and not on the basis of ancillary finding of changes in the ductal system by sialography.

The hazard of injury to the facial nerve should no longer be a deterrent to the performance of parotidectomy when indicated. If the trunk of the facial nerve is exposed as it enters the substance of the parotid gland, that part of the gland superficial to the nerve can be dissected from the trunk and its branches, with direct visualization and little danger of permanent injury to the nerve as mentioned by Beahrs and L'Esperance. There is less danger of injury to the nerve by this method of parotidectomy than there is in enucleating a mixed tumor, for example, because of the direct visualization of the facial nerve from the start. However, in instances of chronic parotitis, the technical diffculties of exposure of the facial nerve are greater because of the pathologic changes in the gland. Nevertheless, parotidectomy can be accomplished without permanent injury to the nerve. Temporary weakness of the facial muscles may be present for a period of a few days to a few weeks, however. This was true in 2 of our cases. In no instance was there permanent injury to the nerve.

In the cases presented, superficial parotidectomy was used in preference to total parotidectomy in 4 of the 6 glands because the former procedure effects relief of symptoms, which is the goal of the operation, and because it can be performed more easily and with less chance of injury to the nerve. Inasmuch as the lesser procedure usually produces the desired result, nothing is to be gained by performing the more extensive procedure. In approximately 200 superficial parotidectomies performed by one of us (Beahrs) for various indications, fistula formation or other difficulty related to the remaining small portion of parotid gland deep to the nerve has not been encountered. It is believed that after superficial parotidectomy this remaining tissue atrophies. In a few instances in which cystic dilatation involves the deep portion of the gland, total conservative (nerve preserved) parotidectomy must be considered, however, as in Cases 1 and 5.

SUMMARY

Some patients with chronic or recurrent parotitis have symptoms of sufficient severity and duration that they do not respond to conservative measures; these patients are candidates for superficial or total conservative parotidectomy. With proper techniques these procedures can be carried out without danger of injury to the facial nerve and with complete relief of symptoms in such patients.

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ETIOLOGY AND TREATMENT OF AMMONIA INTOXICATION ASSOCIATED WITH DISEASE OF THE LIVER

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THE AMMONIA that occurs in the blood originates mainly in the gastrointestinal tract as a result of the action of intestinal bacteria on nitrogenous substrates. These substrates include dietary protein, urea, and uric acid, which are excreted in part into the gastrointestinal tract. Blood that accumulates in the gastrointestinal tract may also be an important source of increased blood ammonia. Although the portal blood normally contains relatively large amounts of ammonia, the liver rapidly removes it, largely by converting it to urea. Consequently there usually is little or no ammonia in the peripheral blood. Small amounts of ammonia have been reported to originate from the lungs, kidneys, and brain, but these sources are quantitatively unimportant in comparison to the ammonia derived from the gastrointestinal tract.

Because the liver has such an important role in the metabolism of ammonia, a decrease in hepatic function, or a bypass of the liver brought about by the development of portal-systemic collaterals or surgical shunting procedures may cause high levels of ammonia to accumulate in the peripheral blood.

A relationship between increased blood ammonia levels and hepatic coma is becoming more apparent as clinical and experimental knowledge of ammonia metabolism increases. The consistent occurrence of significantly elevated levels of ammonia in the blood of patients with "hepatic coma," and the clearing of the sensorium that follows a reduction in the ammonia levels both indicate that ammonia intoxication is an important factor in the production of hepatic encephalopathies. Further confirmation of an etiologic role of ammonia in hepatic coma is to be found in the fact that this syndrome can be reproduced in both experimental animals and human subjects by increasing the blood ammonia, either by the administration of ammonium salts or by the feeding of high protein diets or urea. "Hepatic coma" is a frequent complication in patients who have had vascular shunting procedures performed for portal hypertension or in those patients in whom chronic liver disease is associated with gastrointestinal hemorrhage.

The use of measures to combat ammonia intoxication is of great urgency because neurologic damage may be irreversible when the central nervous system is subjected to prolonged exposure to a high blood ammonia. The treatment of ammonia intoxication is directed toward reducing the amount of ammonia entering the portal circulation and lowering the levels of ammonia in the systemic blood. The production of ammonia in the gastrointestinal tract of patients with severe liver disease can be controlled by (1) limitation of the intake of protein, (2) control of gastrointestinal bleeding, (3) prompt removal by catharsis or lavage of blood which may have accumulated from hemorrhage, and (4) oral administration of antibiotics to diminish the numbers and activities of the intestinal bacteria which produce ammonia from nitrogenous substrates. Furthermore, the administration of ammonium

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salts or of resins containing ammonium or diamox®[1] must also be avoided in these patients.

In order to decrease the amount of nitrogenous substrates in the gastrointestinal tract, complete removal of protein from the diet is essential during the acute phase of ammonia intoxication. Following the acute phase dietary protein may be increased gradually as tolerated by using as a criterion of tolerance the effect of the additional protein on the blood ammonia. In cases of chronic ammonia intoxication secondary to surgically constructed vascular shunts, or large portal systemic collateral shunts in association with long standing cirrhosis, it may be necessary to maintain a decreased protein intake permanently to avoid a recurrence of symptoms. In such cases the dietary protein intake need not exceed ½ gram per kilogram of body weight. A positive nitrogen balance may be maintained at this reduced level of dietary protein if all of it is of nutritionally excellent quality.

When gastrointestinal hemorrhage is the cause of ammonia intoxication the source of bleeding must be sought and controlled. This may be difficult because even though the diagnosis of severe liver disease has been established, the exact source of the bleeding may not be known. In addition to the history and physical examination, an emergency gastrointestinal study by x-ray films or an esophagoscopy (if these procedures are possible) may be needed to establish the diagnosis. When a diagnosis of bleeding esophageal varices is made or strongly suspected, treatment with the Sengstaken esophageal compression balloon should be attempted. Surgical control of bleeding esophageal varices may have to be done as an emergency procedure if the bleeding has not been controlled by esophageal tamponade. Other causes of gastrointestinal hemorrhage, such as peptic ulceration, hemorrhoids, neoplastic disease, and blood dyscrasias, should be treated with appropriate methods if continued bleeding which cannot be controlled by conservative measures occurs. Regardless of the cause of bleeding, the blood accumulated within the gastrointestinal tract must be removed as soon as possible. For this purpose, gastric lavage and enemas are effective. During the acute phase of ammonia intoxication, the removal of blood from the gastrointestinal tract can also be expedited by the use of a mild cathartic such as 30 cubic centimeters of milk of magnesia 4 times daily administered by indwelling nasogastric tube.

The oral administration of antibiotics to reduce the intestinal flora is as important as the other measures used for control of ammonia production within the gastrointestinal tract. Neomycin appears to be the most effective antibiotic for this purpose. It should be given orally or by nasogastric tube in doses of ½ to 1 gram every 6 hours. The clinical and biochemical response of the patient will determine the duration of neomycin therapy. This period is usually between 4 and 7 days. Examination of the patient's urinary sediment should be done daily to detect promptly the occurrence of manifestations of nephrotoxicity. In some cases an enema of neomycin may be an effective method for rapid intestinal sterilization.

Although control of the production of ammonia in the gastrointestinal tract is effective for the treatment of ammonia intoxication, a rapid lowering of the blood ammonia is essential to prevent irreversible brain damage when the patient is in stupor or coma. Methods to lower the blood ammonia have usually involved attempts to enhance the reactions by which ammonia is metabolized and removed from the body. The rationale for therapy of ammonia intoxication with glutamic acid proposed by Walshe and by McDermott is based on removal of ammonia by amidation of glutamic acid to form glutamine; however, the results of glutamic acid therapy have been equivocal. Recently, aspartic acid has been

[1]Dawson and associates have suggested that diamox® raises the blood ammonia by impairing the uptake of ammonia by peripheral tissues.

tried for the treatment of ammonia intoxication based on the same biochemical rationale and with similarly discouraging results.

The formation of urea is, quantitatively, the most important method by which ammonia is removed from the body. Although this reaction occurs only in the liver, investigation has shown that experimental removal of 80 to 90 per cent of the liver does not significantly alter urea production. Similar findings were reported in experiments in which livers removed from dogs were perfused with toxic agents. The extreme degree to which hepatic function must be reduced before urea production is affected was confirmed clinically by the ability of arginine to lower blood ammonia significantly and to raise the blood urea in patients with what has been described as "massive hepatic necrosis" (6).

In this laboratory it has been demonstrated that intravenously administered arginine significantly lowers high levels of ammonia in the blood, both experimentally (3) and clinically (6). Comparative studies (7, 8) of the effectiveness of arginine and of glutamic acid in the treatment of experimentally induced ammonia intoxication confirmed the superiority of arginine in lowering high blood ammonia levels rapidly and effectively. The decrease in the level of ammonia in the blood following the administration of arginine was always accompanied by a significant rise in the blood urea nitrogen, suggesting that arginine exerts an effect on the blood ammonia because of its role as a precursor of ornithine in the Krebs-Henseleit cycle in the liver (Fig. 1).

The following case reports are based on the results obtained in the treatment of 50 patients[2] with elevated blood ammonia originating from a variety of clinical situations and associated with varying degrees of encephalopathy, and particular reference has been made to the therapeutic effectiveness of arginine. These patients may be classified according to the cause of ammonia intoxication: (1) patients with exogenous ammonia intoxication from oral ingestion of ammonium salts, diamox®, or from ammonium chloride given intravenously to correct alkalosis; (2) patients with portal cirrhosis associated with an increase in nitrogenous substrates in the intestine as a result either of a high protein diet or of gastrointestinal hemorrhage (most frequently due to esophageal varices); (3) patients who have had surgical shunting procedures performed for the relief of portal hypertension secondary to intrahepatic or extrahepatic venous obstructions; (4) patients with acute hepatic insufficiency as a result of viral hepatitis or ingestion of hepatotoxins.

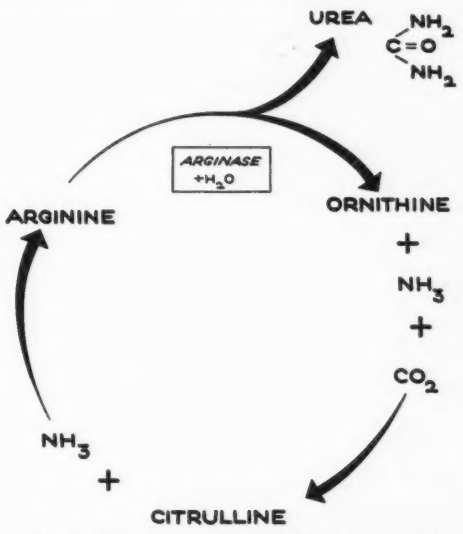

FIG. 1. Essential components of the urea cycle. Arginine, under the action of liver arginase, forms urea and ornithine. This latter compound, accepting a mol of ammonia and carbon dioxide, is converted to citrulline, which in turn accepts a second mol of ammonia to reform arginine. Thus, in the course of this cycle, for each mol of urea formed, 2 mols of ammonia are simultaneously removed.

In order to evaluate the clinical response to the treatment of ammonia intoxication, the various degrees of encephalopathy were

[2]These patients were treated in the University of California Hospital, the San Francisco Hospital, Franklin Hospital, the United States Public Health Service Hospital, San Francisco, and in the Veterans Administration Hospitals, San Francisco and Oakland.

TABLE I.—A CLINICAL CLASSIFICATION OF ENCEPHALOPATHY ASSOCIATED WITH AMMONIA INTOXICATION

Stage	*Grade*	*State of consciousness*	*Motor activity*	*Reflexes*
Delirium	1.0	Mental confusion. Dysarthria	Increased restlessness	"Brisk" reflexes. Flexor plantar response
	1.5	Irrational behavior. Drowsiness	Development of typical "flap"*	Increased activity (exaggerated reflexes). Positive grasp reflex
Stupor	2.0	Lethargy	Hypertonic	Hyperactive
	2.5	Somnolent, but arousable by vocal or light stimuli	Paratonic rigidity with marked "flap" in both hands and feet. Occasional convulsion	Clonus—ankle and occasionally knee. Extensor plantar response
Coma	3.0	Arousable only by deep painful stimuli	Hypotonic	Hypoactive
	3.5	Unarousable	Flaccid	Absent

*Liver "flap" has been described as a rapid and arrhythmic flexion-extension of the fingers at the metacarpophalangeal joint and flexion-extension at the wrist. In more severe cases there are flexion-extension movements at the elbow and the shoulder with the arms outstretched.

TABLE II.—CLINICAL FEATURES OF A SERIES OF PATIENTS WITH EXOGENOUS AMMONIA INTOXICATION

No., age, and sex	*Diagnosis*	*Precipitating factors*	*Clinical stage* —Grade—* *Initial*	*Final*	*Blood ammonia, —μgm./100 ml.— Initial*	*Final*	*Amount of arginine, grams*	*Duration of treatment, hours*
1 57, M	Portal cirrhosis with ascites and peripheral edema	NH_4Cl and diamox	2.0	1.0	167	76	50	4
2 62, F	Portal cirrhosis with ascites and peripheral edema	NH_4Cl and diamox	2.0	1.0	194	53	50	5
3 71, M	Congestive heart failure (cardiac cirrhosis)	NH_4Cl	2.5	1.0	172	107	25	2
4 76, M	Congestive heart failure (cardiac cirrhosis)	NH_4Cl	3.0	1.0	210	122	50	4
5 68, M	Congestive heart failure (cardiac cirrhosis)	NH_4Cl	2.5	1.0	168	113	25	3
6 47, M	Duodenal ulcer with pyloric obstruction and hypochloremic alkalosis. Portal cirrhosis	NH_4Cl (intravenous)	3.0	1.0	224	95	50	5

*See Table I.

classified into "stages," according to the observed clinical status of the patient with regard to consciousness, motor activity, and deep tendon reflexes. Thus, the patients were described as delirious, stuporous, or comatose. It was also possible to subdivide these clinical stages by the use of numerical "grades." These clinical stages of ammonia intoxication as classified in Table I may be correlated with the neurologic findings in patients with hepatic coma.

For the immediate treatment of ammonia intoxication, arginine hydrochloride was given intravenously. Each dose consisted of 500 cubic centimeters of a 5 per cent solution of arginine in 10 per cent dextrose administered over a 2 hour period. In the early phase of this study, a second dose was given after 4 hours, but later at least 8 to 12 hours were allowed to elapse before the second dose was given, because it was found that serum arginine levels remained high for 8 to 12 hours after the intravenous administration of 25 grams of the amino acid.

The concentration of ammonia in the peripheral venous blood was determined by the microdiffusion technique of Conway; the urea nitrogen of the blood was determined by the manometric method of Van Slyke and Kugel. Serum arginine determinations were made by microbiologic assay or by column chromatography.

Thirty-five of the 50 patients reported in this series were initially in coma but a significant clinical improvement followed treatment in all except 2 of the cases, as indicated by their progression to clinical "grade 1." Levels of ammonia in the blood

TABLE III.—CLINICAL FEATURES OF A SERIES OF PATIENTS WITH PORTAL CIRRHOSIS

No., age, and sex	Precipitating factor	Clinical stage* —Grade— Initial	Clinical stage* —Grade— Final	Blood ammonia —μgm./100 ml.— Initial	Blood ammonia —μgm./100 ml.— Final	Amount of arginine, grams	Duration of treatment, hours	Comment
7 71, M	Esophageal varices	2.0	1.0	139	37	50	24	Discharged for eventual vascular shunt
8 42, M	Esophageal varices	2.5	1.0	147	116	25	1.5	Discharged for eventual vascular shunt
9 58, F	Esophageal varices	2.0	1.0	174	142	25	2	Discharged for eventual vascular shunt
10 52, F	Esophageal varices	2.0	1.5	186	132	25	1.5	Died from hemorrhage next day
11 48, M	Esophageal varices	3.5	2.0	184	62	50	20	Died from hemorrhage next day
12 45, M	Esophageal varices	3.0	2.0	193	128	50	8	Died in coma 3 days later
13 63, M	Esophageal varices	3.0	1.5	224	118	50	12	Discharged for eventual vascular shunt
14 38, F	Esophageal varices	2.5	1.0	178	122	25	4	Died 1 week later from hemorrhage
15 44, M	Esophageal varices	2.5	1.5	202	105	50	16	Died from hemorrhage
16 54, F	Esophageal varices	2.5	1.0	155	76	50	14	Died from hemorrhage 14 days later
17 59, M	Esophageal varices	3.0	1.5	186	122	50	8	Varices ligated
18 37, M	Esophageal varices	3.0	2.5	237	154	25	6	Died from hemorrhage
19 64, M	Esophageal varices	3.0	1.0	212	124	75	18	Died 2 weeks later from hemorrhage
20 47, F	Esophageal varices	3.0	1.5	176	104	50	10	Vascular shunt
21 61, M	Esophageal varices	2.5	1.0	166	92	25	6	Discharged for eventual vascular shunt
22 56, F	Esophageal varices	2.0	1.0	144	68	50	12	Died from hemorrhage 3 weeks later
23 52, M	Esophageal varices	2.5	1.5	196	134	25	4	Vascular shunt
24 50, M	Duodenal ulcer	2.5	1.0	172	114	50	8	Hemorrhage stopped. Patient discharged
25 63, M	Duodenal ulcer	2.0	1.0	157	106	25	2	Gastric resection
26 36, F	Duodenal ulcer	3.0	1.5	206	145	50	12	Gastric resection
27 71, M	Duodenal ulcer	2.5	1.5	162	122	25	3	Stopped bleeding. Patient refused operation
28 55, M	Gastritis	2.0	1.0	176	132	25	4	Conservative therapy. Hemorrhage stopped
29 72, F	Cancer of right colon	2.5	1.5	162	102	50	14	Died of myocardial infarct 2 weeks later
30 53, M	Gastrointestinal bleeding—undetermined etiology	2.0	1.0	154	121	25	2	Conservative therapy. No further bleeding
31 46, F	Hemorrhoids	2.5	1.5	189	112	50	14	Hemorrhoidectomy
32 75, M	Hemorrhoids	2.0	1.5	145	108	25	3	Hemorrhoidectomy
33 53, M	Paracentesis	2.5	1.0	192	130	25	4	Eventually discharged
34 69, M	Paracentesis	2.5	1.5	152	114	25	2	Died from hemorrhage from esophageal varices 5 days later

*See Table I.

were elevated in all cases but following treatment with arginine a prompt reduction in blood ammonia occurred. Fourteen (28 per cent) of the patients in this series died, 9 of whom had portal cirrhosis and bleeding esophageal varices.

Prior to treatment the concentration of ammonia in the blood was correlated with

TABLE IV.—CLINICAL FEATURES OF A SERIES OF PATIENTS WITH SURGICAL SHUNTS

No., age, and sex	*Type of shunt*	*Precipitating factors*	*Clinical stage* —Grade— Initial*	*Final*	*Blood ammonia —μgm./100 ml.— Initial*	*Final*	*Amount of arginine, grams*	*Duration of treatment, hours*
35, M	Portacaval	Postoperative bleeding	3.0	1.5	224	140	50	8
36, M	Portacaval	Unrestricted diet (high protein)	2.0	1.5	174	138	25	2
37, M	Portacaval	Unrestricted diet (high protein)	2.5	1.0	260	164	50	6
38, F	Splenorenal	Unrestricted diet (high protein)	2.0	1.0	311	119	75	16
39, F	Splenorenal	Unrestricted diet (high protein)	1.5	1.0	161	112	25	2
40, M	Splenorenal	Operation	2.5	1.0	234	142	50	9
41, M	Splenorenal	Gastrointestinal hemorrhage	2.5	1.0	261	114	50	12
42, F	Splenorenal	Gastrointestinal hemorrhage	2.0	1.0	237	152	25	2
43, F	Splenorenal	Operation	2.0	1.5	248	176	25	4

*See Table I.

TABLE V.—CLINICAL FEATURES OF A SERIES OF PATIENTS WITH ACUTE HEPATIC INSUFFICIENCY

No., age, and sex	*Diagnosis*	*Total bilirubin, mgm./100 ml.*	*Clinical stage* —Grade— Initial*	*Final*	*Blood ammonia, —μgm./100 ml.— Initial*	*Final*	*Amount of arginine, grams*	*Duration of treatment, hours*	*Comment*
44, 35, M	Homologous serum jaundice	22	3.5	1.0	196	79	50	36	Alert in 36 hours. Taking full protein diet within 1 week
45, 24, M	Homologous serum jaundice	26	3.5	1.0	173	44	75	24	Alert in 48 hours. Recovery in 7 to 10 days
46, 42, F	Homologous serum jaundice	18	3.5	1.0	181	62	75	72	Alert in 40 hours. Recovery complete
47, 51, F	Homologous serum jaundice	25	3.5	1.0	162	37	100	72	Alert in 24 hours.
48, 58, M	Infectious hepatitis	27	2.5	1.5	123	66	25	2	Alert in 12 hours, but slowly relapsed into coma; died 5 days later without further treatment
49, 70, F	Homologous serum jaundice with metastatic lymphosarcoma	29	3.5	1.5	157	129	25	2	Patient awake, but lethargic in 12 hours. Died 12 hours later of widespread metastases and in hepatic coma
50, 30, M	Ingestion of carbon tetrachloride and alcohol	24	2.5	1.0	300	112	125	120	Patient had acute renal insufficiency which was also treated. Patient left hospital 1 month after entry and remained well

*See Table I.

the severity of the neurologic disturbances in more than 95 per cent of the cases. However, following the reduction in blood ammonia neurologic improvement was delayed in those cases in which the ammonia intoxication had been present for a long period. These findings are in accord with those of Phear and associates, who found a 90 per

cent correlation between the concentration of ammonia in the blood and the neurologic state of the patient in 360 blood ammonia determinations made on 66 patients with diseases of the liver.

The description of the results that follows has been arranged according to the four etiologic classifications previously described, because the clinical and biochemical response to therapy varied with each group. The diagnosis and precipitating factors in each case as well as the clinical state and the blood ammonia concentrations prior and subsequent to arginine therapy are summarized in Tables II through V.

EXOGENOUS AMMONIA INTOXICATION (TABLE II)

Ammonium chloride was given orally as a diuretic to 5 patients who had either portal or cardiac cirrhosis; in 3 of these patients the ammonium chloride therapy was combined with diamox®. In the sixth patient ammonium chloride was administered intravenously to correct a hypochloremic alkalosis secondary to pyloric obstruction. In all cases in this group the ammonia intoxication was acute and responded to arginine therapy alone, with clearing of the sensorium and an associated decrease in the blood ammonia within less than 5 hours.

It should be emphasized the ammonium chloride in the usual therapeutic doses may be toxic only in those patients who have impairment of hepatic function, as was true in all the cases listed in Table II.

PORTAL CIRRHOSIS WITH INCREASED NITROGENOUS SUBSTRATES WITHIN THE INTESTINE (TABLE III)

This group of patients presented the most difficult therapeutic problems. Many of them with a clinical grade of less than 2.0 who were in various degrees of delirium were treated successfully with protein restriction, orally administered antibiotics, and control of precipitating factors. However, in many cases the patients were in stupor or coma when first seen, or progressed into stupor in spite of these therapeutic measures. All patients in grade 2 or beyond were immediately treated with 25 grams of arginine every 8 to 12 hours until the clinical state of the patient reverted to less than 2.0.

The most discouraging results were obtained in those patients who were bleeding from esophageal varices. In 15 of the 17 cases, Sengstaken tubes were used to stop the bleeding, which was temporarily controlled in 12 patients; the remaining 3 continued to bleed in spite of esophageal compression and died. Of the group in which hemorrhage was temporarily controlled, 5 patients subsequently died from hemorrhage during the same period of hospitalization. Therefore, a total of 8 out of 15 patients died.

Portacaval shunt procedures were performed on 4 of the remaining 9 patients, with 1 postoperative death and 3 survivors. The other 5 patients were discharged to be prepared for portacaval shunt procedures at a later time when hepatic function had improved. It is possible that immediate performance of a vascular shunt or ligation of esophageal varices in those cases in which bleeding could not be controlled might have increased their chances of survival, as indicated by Linton and by Welch.

In addition to controlling the bleeding, the blood was removed from the intestine by lavage and catharsis, and oral antibiotic therapy was given along with intravenous arginine therapy. Occasionally after the administration of arginine was discontinued (because at that time the available supply of arginine was limited) the clinical condition of the patients deteriorated rapidly and there was an associated rise in blood ammonia.

In 9 other cases bleeding was secondary to peptic ulceration, gastritis, or disease of the colon. The prognosis in this group of patients would be expected to be better than in those with esophageal varices because in this latter group there is usually a greater degree of liver damage. Furthermore, the procedures used in the management of these

surgical cases of gastrointestinal hemorrhage are more clearly established.

In 2 cases coma or stupor were precipitated by paracentesis. Minor disorders of consciousness (delirium) and an increase in blood ammonia have been observed following this procedure. This reaction may be attributed to the hyponatremia and hypotension and a resulting probable hepatic ischemia which may follow paracentesis.

SURGICAL SHUNTING PROCEDURES (TABLE IV)

In these patients the blood ammonia was continuously maintained at a higher than normal level because of the shunting of portal blood into the systemic circulation, and also because the reduced blood supply of the liver retarded hepatic clearance of blood ammonia. These patients often had a clear sensorium although the blood ammonia was in a range comparable to that which would result in stupor in cirrhotic patients or coma in normal subjects. Furthermore, the blood ammonia in these patients characteristically fluctuated rapidly; a slight increase in dietary protein or a minor episode of gastrointestinal bleeding might be sufficient to cause an increase in the blood ammonia, with associated significant changes in sensorium.

Only 1 death occurred in this group. This occurred following an episode of profuse gastrointestinal hemorrhage from esophageal varices. In every case the blood ammonia was rapidly decreased to normal following arginine therapy and within less than 12 hours all patients had significant clinical improvement. After they recovered from the acute episode of ammonia intoxication the patients were advised to eat low protein diets (40 grams or less per day). Several patients also were given periodic orally administered antibiotic therapy to maintain decreased bacterial flora in the gastrointestinal tract.

Patients 40 and 43 had an immediate rise in blood ammonia with accompanying stupor during the early postoperative period but responded well to arginine therapy. The cause of coma following operative procedures without gastrointestinal bleeding might have been related in these 2 cases to hepatic ischemia induced by a temporary period of hypotension during the procedure.

ACUTE HEPATIC INSUFFICIENCY (TABLE V)

The results of treatment in this group of patients were the most successful. This might be expected because all these patients presumably had normal hepatic function prior to the onset of acute hepatic insufficiency. Six patients had viral hepatitis with "massive hepatic necrosis." The seventh had acute hepatic insufficiency following the ingestion of carbon tetrachloride. All except the last patient lapsed into deep coma with Cheyne-Stokes respirations. The rise in blood ammonia was in no case greater than 200 micrograms per cent, a level which does not seem consistent with the severity of the associated symptoms. However, it seems likely that even a moderate increase in blood ammonia may be the cause of toxicity when it occurs rapidly in one who has not previously been subjected to high levels of ammonia in the peripheral blood. The rise in the blood ammonia may be attributed to dilatation of portal system channels following marked atrophy of the liver, as well as to massive hepatic destruction.

The results of therapy in these patients suggest that ammonia intoxication may be a potentially serious finding in the early stages of acute hepatic insufficiency. For this reason control of ammonia intoxication is an important requisite early in the management of these patients. This fact is emphasized by the survival of 5 of the 7 comatose patients with "massive hepatic necrosis" who were treated with arginine.

SUMMARY

The ammonia in the peripheral blood is derived largely from the gastrointestinal tract as a result of the action of bacteria within the colon on nitrogenous substrates, including blood which accumulates secondary to gastrointestinal hemorrhage.

The treatment of ammonia intoxication is designed to reduce the amount of ammonia entering the portal circulation as well as to lower the levels of ammonia in the systemic blood.

The production of ammonia within the gastrointestinal tract in patients with severe disease of the liver can be controlled by: (1) limitation of the intake of protein; (2) control of gastrointestinal bleeding; (3) prompt removal, by catharsis or lavage, of blood which may have accumulated from hemorrhage; (4) oral administration of antibiotics to diminish the numbers and activity of the intestinal bacteria that produce ammonia from nitrogenous substrates.

Control of the production of ammonia in the gastrointestinal tract is effective in the treatment of ammonia intoxication. When the patient is in stupor or coma a rapid lowering of the blood ammonia is essential to prevent irreversible brain damage. The methods used to lower the blood ammonia are directed toward enhancing the reactions by which ammonia is normally metabolized in the body; these include amidation of glutamic acid or aspartic acid, and the formation of urea which is accelerated by arginine.

Fifty patients were treated for ammonia intoxication originating from a variety of clinical situations, such as: (1) exogenous ammonia intoxication, (2) portal cirrhosis associated with gastrointestinal hemorrhage, (3) surgical shunting procedures, or (4) acute hepatic insufficiency. With the addition of arginine to other therapeutic measures used for ammonia intoxication all except 2 of 50 patients initially improved clinically and biochemically, even though 35 of them were first seen in deep coma. Only 14 (28 per cent) of the patients died in this series, 9 of whom had portal cirrhosis and bleeding esophageal varices.

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A CLINICAL EVALUATION OF MALIGNANT MELANOMA

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MALIGNANT MELANOMA has been the subject of increasing interest over the years because of its dramatic and often enigmatic behavior. The continuing appearance of patients who must suffer because of unwarranted delay in diagnosis and inadequate treatment justifies another critical study of clinical experience and further analysis of the important points of diagnosis and treatment. In addition, the dilemma regarding the extent of radical treatment calls for presentation of a series in which treatment methods have remained relatively constant over a significant period of time.

From 1937 through 1956, 26,509 patients were referred to the Robert Winship Memorial Clinic. Of these, 35.6 per cent were found to have cancer. Melanoma was found in 253 patients, the frequency thus being 0.95 per cent of all patients seen or 2.7 per cent of patients with cancer. A number of these were included in an earlier report by Trincher and associates.

The diagnosis of malignant melanoma was confirmed histologically in 236 instances (92.9 per cent). Of the 18 patients without histologic confirmation, 17 were seen in consultation only, and the original diagnosis was made elsewhere. Histologic specimens were not available for examination but physicians' reports or clinical evidence indicated malignant melanoma. In the other patient without histologic diagnosis distant metastases were present with numerous pigmented nodules scattered over the body.

POSSIBLE FACTORS IN THE DEVELOPMENT OF THE DISEASE

The records were searched in an attempt to discover some environmental or hereditary factors common to this group of patients. Such factors as complexion, family history of cancer, blood types, and history of trauma to a mole were noted.

Complexion was not stated frequently enough to be of any value. A family history of cancer was found in 42 of 158 (26.6 per cent) instances in which this information was available. In a group of 209 patients seen with no cancer 91 (43.5 per cent) had a family history of cancer. In another group of 214 patients with cancer at various sites, 76 (35.5 per cent) had a familial history of cancer. Although the difference between the study group and the no cancer group is significant, the fact that the patients in the no cancer group were queried over the past 2 years and those of the malignant melanoma group during the past 20 years introduces a bias which may be of importance. However, the point that no greater frequency of cancer was found in the families of patients with malignant melanoma does not support the hypothesis of a hereditary etiologic factor.

Further evaluation of a hereditary factor was attempted when blood types were studied. Since no special effort had been made to type every patient, only those operated upon and needing transfusions were available for study. Thirty patients had the following blood groups: group O, 18; group A, 10; group AB, 2. Twenty-six were Rh positive, 4 Rh negative. This ratio does not appear to differ from that stated for the general population.

The evaluation of trauma as an etiologic agent is understandably difficult. In 139 instances a statement in the record concerning trauma or improper local therapy was found. In 97 (69.8 per cent) there was a positive history of such trauma. The fact that in 42 instances (30.2 per cent) there

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was no history of antecedent trauma suggests that some additional factors may initiate a malignant transformation. In 52 instances the trauma consisted of friction, bruising, abrading, or other manipulation of a mole. In 45 instances (32.4 per cent) the patients had received improper local treatment when first seen. The most frequent mistreatment was fulguration or electrodesiccation, 18 times. Some type of ointment or paste had been prescribed 15 times. Local excision of a black mole without histologic examination was done in 6 instances. Two were treated by irradiation without histologic diagnosis, 2 others were treated for eczema and athlete's foot respectively, and 1 pedunculated lesion was treated by a ligature around the base. In many instances, the trauma may have called attention to a mole already undergoing changes in size or color. The influence of trauma on the rapidity of development of regional or distant metastases may be a much more important consideration. Amadon found that metastasis does occur earlier in local melanoma treated by electrodesiccation. Furthermore, he demonstrated histologically widening of lymphatic channels and increased vascularity in the beds of desiccated keratoses. These changes, he postulated, enhanced early dissemination of tumor emboli dislodged and forced along channels by tissue steam.

AGE, SEX, AND BODY DISTRIBUTION

The age and sex distribution is shown in Table I. All patients were white. The sex distribution was about equal (48.4 per cent males and 51.6 per cent females).

Eight patients were prepubertal at the time of diagnosis. One patient had 2 melanomas, one at the age of 5 and the other at age 11 years. Except for 1 seen in consultation all of these prepubertal lesions were treated by local excision and have caused no further trouble. We consider these lesions "juvenile melanomas" as described and categorized by Spitz and Allen(1). They are excluded from any tabulations of end results.

TABLE I.—AGE AND SEX DISTRIBUTION

	Male		*Female*		*Total*	
Age	*No.*	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*
0- 9	2	1.6	3	2.3	5	2.0
10–19	2	1.6	9	6.9	11	4.3
20–29	12	9.8	15	11.4	27	10.6
30–39	23	18.7	33	25.1	56	22.1
40–49	34	27.6	12	9.2	46	18.1
50–59	18	14.7	20	15.3	38	15.0
60–69	22	17.9	19	14.5	41	16.1
70–79	9	7.3	11	8.4	20	7.9
80 plus	1	0.8	9	6.9	10	3.9
Total	123		131		254	

One female age 5 developed new primary at age 11.

Sixty-one per cent of patients were over 40 years of age.

Body distribution of the total group is presented in Table II. More lesions of the head and neck were seen than in other studies, but this observation reflects more the selection of patients rather than any absolute increase in frequency. A somewhat disproportionate number of referrals to our clinic are for conditions of the head and neck.

METHODS OF TREATMENT

The first line of defense in the treatment of malignant melanoma is prevention. It is commonly believed that the majority of these cancers originate in the junctional element of common nevi, particularly when located in uncommon areas as on the palms and soles, genitalia, and in those areas subjected to repeated trauma. We have practiced removal of such nevi by surgical excision using locally injected procaine anesthesia and obtaining a distinct but small margin of normal skin on all sides of the lesion removed. The use of the electrodesiccation apparatus has been avoided in the treatment of junctional and compound nevi because of the possibility of incorrect diagnosis or incomplete treatment. All lesions removed are submitted to the pathologist for microscopic examination. There has been no instance of malignant melanoma developing at the site of local excision of such a nevus or of metastasis occurring from a lesion adjudged benign at the time of removal.

Clinical suspicion that a mole is malig-

TABLE II.—BODY DISTRIBUTION

Primary site		*No.*	*Per cent*
Head and neck (total)		91	35.8
Lip	1		
Eyelids	2		
External ear	11		
Other parts of face	48		
Scalp and neck	29		
Trunk		67	26.4
Upper extremity		41	16.2
Lower extremity		51	20.0
Palate		1	.4
Unknown and unspecified		3	1.2

nant is the first item in the management of malignant melanoma. Change in size, or degree or homogeneity of pigmentation, cracking, weeping, or ulceration in a preexisting mole or the appearance of a new one are all indications of possible malignant growth. Biopsy of such lesions is by complete excision, never by incision, since there is reliable evidence that the latter practice may result in dissemination. In a bulky lesion already ulcerated, however, it seems unlikely that a small incisional biopsy carefully performed would do any harm.

Lesions known to be malignant melanomas are excised with a wide margin of normal skin down to and including underlying fascial structures with as little manipulation and traumatization of the tumor as possible. This procedure is best carried out in the operating room under general anesthesia. The question of "How wide is wide enough?" is pertinent and one for which there is no ready answer. The propensity of malignant melanoma to invade adjacent superficial lymphatics and give rise to satellite nodules makes it desirable to remove a distinct area of normal-appearing skin around the local lesion. The occurrence of multiple foci in a limited area also makes wide excision desirable. There is no landmark to guide the surgeon, but we have essayed to remove 3 to 5 centimeters of skin on all sides of a lesion when feasible. In the majority of instances a skin graft to close the defect has been necessary. The effectiveness of this procedure is indicated by local recurrences in only 3 per cent of the treated patients.

When regional lymphatics are involved, or subsequently become involved after primary treatment, and there is no known distant metastasis, these areas are dissected radically. Thin skin flaps (about ⅛ inch) are made and the regional lymphatic block is meticulously removed. When the primary area is conveniently adjacent to the regional lymphatics this dissection is done in continuity, but no special effort is made to do such a dissection when there is an appreciable distance between the primary lesion and the regional lymphatics. As desirable as excision and lymphatic dissection in continuity may seem in theory, it is likely to be a futile gesture because of the abundance and variable courses of lymphatics intervening between an area some distance removed from the regional nodes. Further, the speed at which tumor emboli, once dislodged from a primary lesion, travel along lymphatic channels is probably relatively rapid.

Amputation of a digit or extremity has been done only in a few instances, as when there was deep invasion of subfascial structures or when there were implants intervening between the primary site and the regional nodes.

Prior to 1951 no "prophylactic" regional lymph node dissections were done. Since that time we have practiced dissection of the regional lymphatics when there was no evidence of clinical disease, provided the primary lesion is so located as to have a definite relationship to a single regional lymph node area. Lesions located near the midline of the trunk may spread to either side and up or down, and hence do not lend themselves to such treatment.

Only 3 patients having such prophylactic dissections have been followed up for 5 or more years. Two of these patients had primary lesions on an extremity, and both are well. One with a primary lesion on the trunk died of malignant melanoma. Seven patients had such dissections more than 2 years ago, and of these, 4 are living and apparently free of disease, while 3 are dead of malignant melanoma. Three of the 4 living

had extremity lesions, the fourth lesion was on the trunk; and of the 3 failures, 2 lesions were on an extremity and 1 was on the head. These results are inconclusive, of course, but the results of other workers, are sufficiently encouraging for us to continue this practice in our clinic. It would seem that if one dissects clinically negative lymphatic areas and finds microscopic metastasis the prognosis would be better than if the dissection were delayed perhaps months until palpable, enlarged nodes were found. One must weigh in each instance what might be gained against the added morbidity and even slight mortality involved.

Radiation plays no part in the primary treatment of malignant melanoma, but occasionally distant metastasis, particularly to bone, will respond quite gratifyingly to external irradiation. An occasional patient with generalized disease will respond to chemotherapy. Palliative surgery for removal of potentially ulcerative tumors requires the exercise of considerable judgment but is often a valuable adjunct to treatment. Neurosurgical procedures for the relief of pain are occasionally of value. The palliative treatment of this disease, as in any other, requires a close and sympathetic relationship between doctor and patient, and close attention to the small details of management which make it easier for the patient to live with his disease for the remainder of his time.

Rare reports of apparent spontaneous remission are found but they are all too rare to be anticipated. Because of them we are justified, however, in avoiding a totally hopeless philosophy in managing a given patient. Such a case is herein reported.

CASE REPORT

M. C., a 52 year old white female, was seen for the first time in March of 1949. She had a history of a "blood blister" on the lateral aspect of her right foot the preceding year. When examined she was found to have a fungating papillary lesion in the midportion of the lateral aspect of the right foot, the lower edge of which encroached upon the plantar surface. There were numerous pigmented nodules surrounding this lesion. In April of 1949 a wide excision of the lesion with skin grafting of the defect was completed. The pathologist's report was malignant melanoma. Three weeks later she had a right groin dissection and metastatic melanoma was found in the large nodes from the groin. She was free of disease until March of 1950 when she returned with metastatic nodules on the right side of the thigh. Upon biopsy of one of these, metastatic melanoma was found. She refused any radical procedure and was treated by low voltage x-ray with regression of many of the nodules. The metastatic nodules continued to appear in the skin of the thigh and leg for the next year and she was advised again to have a hip joint disarticulation, which she continued to refuse. She was not seen again until March of 1953 when she had only 1 recurrent nodule just above the knee in the lateral aspect of the right leg. In October of 1953 she developed another lesion just above the right external malleolus. Both of these lesions were excised locally. She had no further lesions until June of 1954, when numerous nodules were observed scattered over the right leg. One was excised and found to be metastatic melanoma. While 22 skin nodules which received 2,000 roentgens each regressed, it was observed that some untreated ones also disappeared. She has had no new lesions since July of 1954 and was last seen in May of 1957 with no evidence of recurrence.

TABLE III.—FIVE YEAR RESULTS

Status	*Local*	*Regional metastasis*	*Distant metastasis*	*Total*
Alive				
With cancer	6	4		10
Without cancer	30	5		35
Recurrence	5	3		
No recurrence	25	2		
Status unknown	0	0		0
Total	36	9	0	45
Dead				
With cancer	21	18	2	41
Without cancer	6	2		8
Status unknown	1	0		1
Total	28	20	2	50
Grand total	64	29	2	95

RESULTS

In reporting end results care must be taken to define terminology. Two terms are used; while "survival rate" refers to the total number of patients living divided by the total number treated over a specific time period, "5 year definitive cures" refers to those patients living free of cancer at the end of 5 years, divided by the total number treated less those lost to follow-up and those dead of other causes. One must understand that the term "cures" is not absolute as can

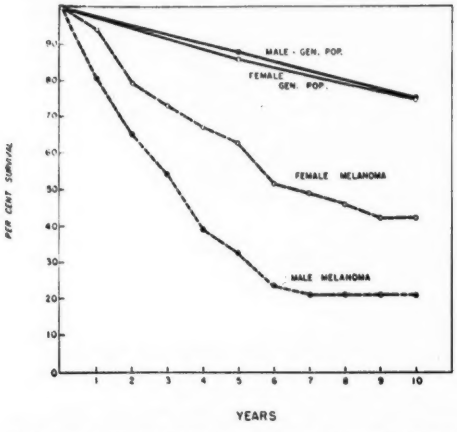

FIG. 1. Survival rates for patients with malignant melanoma compared to expected survival for white males and females.

be seen in Figure 1, but it does provide a measure for comparison with other studies.

Patients receiving treatment elsewhere prior to their visit to the clinic affect end result statistics. Usually those patients with unsuccessful or improper initial treatment are the ones referred. This selection tends to make results appear worse than they really are. Our results include all treated patients with special mention made when indicated of those receiving no previous treatment.

Excluding the 9 "juvenile melanomas" 245 patients were seen. Seventy-four received no treatment, being seen only in consultation. Of the remaining 171 patients, 36 were treated less than 2 years ago, 40 between 2 and 5 years ago, 52 between 5 and 10 years ago, and 43 over 10 years ago. None of our patients were lost to follow-up; all were seen or contacted sometime in 1956 or early 1957.

Ten year group. In Figure 1 the 10 year survival rates for each sex are plotted against the expected survival of a similar number (95) and age group taken from U. S. Life Tables for 1939 to 1941. Calculations were made by standard actuarial methods as described by Berkson and Gage. In the general population the males and females were similar, both having a 75 per cent chance of living 10 years after 1939 to 1941. However, in the cancer group the females have a 42 per cent chance of living 10 years after diagnosis but the males only a 21 per cent chance. Pack reported better results in women also.

The over-all 10 year survival rate is 26 per cent. When these patients dead of causes other than cancer are excluded the 10 year definitive cure rate is 31 per cent.

Slides from 7 of the 11 patients living 10 or more years were available for restudy. Pathology reports were available on the remaining 4. Seven patients had superficial melanomas. One of these was first seen in 1946 with a malignant melanoma of the left leg. Three years later a recurrence developed in the skin near the previous excision and another recurrence the next year. Both recurrences were treated with wide excision and skin graft. She has been free of disease for 7 years. We have frequently observed the efficacy of energetic treatment of even wide local recurrence.

Two patients had invasion of the dermis and are free of cancer after more than 10 years. Both lesions were under 2 centimeters in size, 1 measuring 1.7 centimeters and the other measuring 1 centimeter in greatest diameter.

Two patients with regional metastases are alive and well 10 years after treatment. One, a woman 74 years of age, had a melanoma of the right cheek with cervical nodes present. A wide excision and neck dissection were done and the patient had no recurrence. The other, a male, aged 31 years, had a melanoma of the right thigh. He had had an excision just prior to his first visit and the wound was severely infected. He was observed for 6 months and nodes developed in the inguinal region. He had a radical groin dissection in 1946 and has continued to be well. Both patients had metastatic melanoma in lymph nodes. Despite a prognosis poor by all criteria, energetic treatment is worth while and mandatory.

Five year group. The over-all 5 year survival rate is 47 per cent, 45 of 95 living for 5 or more years after treatment (Table III). Ten patients had evidence of recurrence or metastasis and 9 of the dead patients died of other or unknown causes without clinical evidence of cancer at the time of death. Therefore the 5 year definitive cure rate is 41 per cent (35 out of 86) as indicated in Table IV.

The 5 year definitive cures by stage of disease is as follows: local 53 per cent, regional metastasis 19 per cent, distant metastasis 0 per cent. When those patients receiving some treatment previous to their treatment in the Winship Clinic are excluded the 5 year cures are local 57 per cent, with regional metastasis 25 per cent, with distant metastasis 0 per cent. The over-all 5 year definitive cures of those patients who were treated only at the Winship Clinic is 53 per cent.

More women are cured than men, 56 per cent of all the women, and 61 per cent of women treated only by us were free of cancer at 5 years. In contrast 24 per cent of all the men and 41 per cent of those treated only by us were considered cured at 5 years after treatment. This sex difference is significant (P=.0065) when the total numbers are used but the difference is not large enough to be other than suggestive in the cases treated only at Winship Clinic. Among all cases, when the stage of disease is localized or limited to regional metastasis, women experienced a higher cure rate than men (Table IV).

Two to 5 year group. In 40 patients diagnosis was made and treatment given between 2 and 5 years ago. Sixty per cent survived at least 2 years after treatment. Seventy-one per cent of these patients with local involvement survived whereas only 33 per cent of those with regional metastasis survived. Although the survival rates were consistently higher for the women and for the group receiving no previous treatment the differences are merely suggestive, not statistically significant.

TABLE IV.—5 YEAR DEFINITIVE CANCER CURES

	All cases			*Primary cases*		
	No. of patients	*No. cured*	*Per cent cured*	*No. of patients*	*No. cured*	*Per cent cured*
Local						
Male	24	8	33	18	8	44
Female	33	22	67	29	19	66
Total	57	30	53	47	27	57
Regional						
Male	15	2	13	4	1	25
Female	12	3	25	4	1	25
Total	27	5	19	8	2	25
Distant						
Total (male)	2	0	0	0	0	0
Grand total	86	35	41	55	29	53

SIGNIFICANCE OF DEGREE OF INVASION

The patients with local disease were divided into those whose condition was diagnosed histologically as superficial malignant melanomas and those having invasive malignant melanomas. Invasion of the dermis constituted the line of division. Eight of the 14 patients with superficial lesions were alive and free of cancer 5 years after treatment (57 per cent) (Table V). Among the 38 with invasive lesions 15 (40 per cent) were cured. No sex differences existed in the cures in the superficial group. However, in the invasive group 55 per cent of the women and only 19 per cent of the men were free of cancer 5 years following diagnosis. Although not significant at the 5 per cent level (P=.058), this difference is suggestive. Lund and Ihnen reported 75 per cent of superficial lesions and 23 per cent of invasive lesions cured. Allen and Spitz(2) reported 74.1 per cent 5 year cures of 27 patients with superficial malignant melanomas of the skin. Neither group reported separate rates for the sexes in superficial lesions. Allen and Spitz reported a significantly better prognosis for women in the

TABLE V.—SIGNIFICANCE OF DEGREE OF INVASION (5 YEAR RESULTS)

	Total patients	*Total cures*	*Per cent cures*
Superficial			
Male	7	4	57
Female	7	4	57
Total	14	8	57
Invasive			
Male	16	3	19
Female	22	12	55
Total	38	15	40

All patients had local disease when first seen.

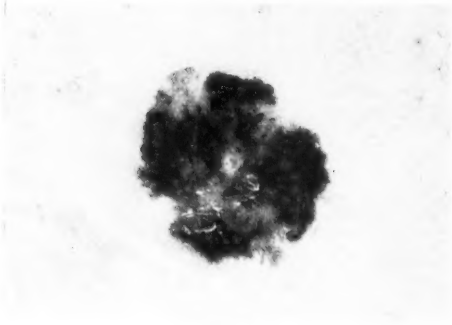

FIG. 2.

invasive group. Our results do not vary from those reported elsewhere.

In general, the prognosis is better for both sexes if the lesion has not invaded the dermis. However, it is a known fact that widespread metastases do occur from superficial lesions (Fig. 2).

SIGNIFICANCE OF BODY DISTRIBUTION

Table VI shows the 5 year definitive cures by body distribution for males and females. Because of the small numbers only 4 categories were used. As can be seen more women were cured in each category. The best results were in upper extremity lesions (57 per cent). Lund and Ihnen reported 42.9 per cent upper extremity lesions cured, which is their best result. However, Hall and associates reported only 16.2 per cent upper extremity lesions cured. Our poorest results were on the trunk (26 per cent), yet none of our differences is significant at the 5 per cent level. Allen and Spitz report their best results were lesions of the skin of head and neck (40.5 per cent) and their worst, excluding mucous membranes, were on the trunk (15.9 per cent). However, they cured only 25 per cent of the lesions of the upper extremity.

TABLE VI.—SIGNIFICANCE OF BODY DISTRIBUTION (5 YEAR RESULTS)

Site	*Cures*	*Failures*	*Indeterminate*	*Total*	*Per cent cures*
Head and neck					
Male	4	8	6	18	33
Female	7	9	2	18	44
Total	11	17	8	36	39
Trunk					
Male	2	10	0	12	17
Female	3	4	0	7	43
Total	5	14	0	19	26
Upper extremity					
Male	2	5	0	7	29
Female	6	1	0	7	86
Total	8	6	0	14	57
Lower extremity					
Male	2	8	0	10	20
Female	9	6	1	16	60
Total	11	14	1	26	44

Probably because of its variable lymphatic drainage, lesions on the trunk have a much graver prognosis. Our results are comparable with other reports.

SIGNIFICANCE OF SIZE OF LESION AND ULCERATION

In 76 of our determinate cases the size of the primary lesion and the presence or absence of ulceration was stated on the record. As can be seen in Table VII in those lesions less than 2 centimeters in diameter and with ulceration results were poorest. Allen and Spitz reported a significantly greater number of smaller lesions, that is, less than 2 centimeters among the survivors than among the nonsurvivors. In addition, they found a greater frequency of ulceration among the fatalities. Tompkins found ulceration indicated a poorer prognosis and that patients with the largest ulcerated lesions bore the worst chances of cure. Lund and Ihnen found patients with lesions 2 centimeters or less in size to have the best prognosis although they made no statement concerning the presence of ulceration.

Our data suggest that the patient with a small lesion with ulceration bears the poorest prognosis. However, we could not support the opinion that size per se is of prognostic significance. The possibility does exist that the same factor which is responsible for early dissemination causes early ulceration.

DISCUSSION

These cure rates found in our material have both surprised and pleased us. We do not attribute them to any superior technique

TABLE VII.—SIGNIFICANCE OF SIZE AND ULCERATION (5 YEAR RESULTS)

	Primary lesion less than 2 cm.			*Primary lesion more than 2 cm.*			*Total*		
	No. patients	*No. cures*	*Per cent cures*	*No. patients*	*No. cures*	*Per cent cures*	*No. patients*	*No. cures*	*Per cent cures*
Without laceration									
Male	20	6	30	5	1	20	25	7	28
Female	25	12	48	8	5	63	33	17	52
Total	45	18	40	13	6	46	58	24	41
With ulceration									
Male	6	0	0	4	1	25	10	1	10
Female	3	0	0	5	3	60	8	3	38
Total	9	0	0	9	4	44	18	4	22
Total									
Male	26	6	23	9	2	22	35	8	23
Female	28	12	43	13	8	61	41	20	49
Grand total	54	18	33	22	10	45	76	28	37

of treatment nor consider them necessarily exceptional. We believe similar results can be obtained by anyone with a full clinical acquaintance of melanoma, a high degree of suspicion and respect for its potentialities, and a both realistic and optimistic philosophy regarding its treatment. When compared with the prognosis in many other malignant processes that in melanoma is far from the most dismal.

Fortunately, we were able to follow-up all patients for this study. Based on previous experience we believe that a 100 per cent follow-up contributes toward a higher salvage rate since ordinarily those patients who are lost to follow-up are considered in the tabulated material as dead of the disease.

SUMMARY

The 253 patients seen at the clinic during the past 20 years with the diagnosis of malignant melanoma comprise the subject of this report. The records were reviewed to determine the significance of several factors in the development of the disease. The role of heredity and trauma in the development of malignant melanoma remains obscure. Age, sex, and body distribution of the lesions are given. Our method of treatment, which until recently has been more or less uniform over the period of the study, is presented. A case of apparent spontaneous remission is reported. Our 5 and 10 year definitive cure rates are 41 per cent and 31 per cent, respectively.

The prognosis is uniformly better for women. This holds true when the sexes are matched as to stage of disease, size and location of lesions, and presence of ulceration. When the superficial melanomas are considered the prognosis is equally good for both sexes, but when the tumor invades the dermis the prognosis again is better for women. Some other factor must determine the better prognosis for women. Lesions which have not metastasized to regional lymph nodes bear a better prognosis. We found that ulceration, and particularly ulceration in small lesions, indicates a poor prognosis. Superficial melanomas, although the prognosis is better, are potentially as dangerous as invasive lesions and should be treated as fully malignant melanomas. Tumors arising on the trunk involve a poorer prognosis than lesions which are encountered about the head or the extremities. Wide local excision including the removal of the underlying fascia remains the most effective treatment.

CONCLUSIONS

1. Early, intelligently conceived, forthright, and consistent treatment of melanoma is surprisingly efficacious.

2. The value of prophylactic node dissection of the appropriate lymphatics, while theoretically probable and inferred by accumulating evidence, does remain to be proved.

3. A more hopeful outlook regarding melanoma is justified.

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A NEW APPROACH TO THE ANORECTAL FISTULOUS ABSCESS BASED ON THE HIGH INTERMUSCULAR LESION

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THE AUTHOR, in 1953 (3) first drew attention to a high anorectal abscess situated between the internal anal sphincter, medially, and the longitudinal muscle together with the external anal sphincter, laterally (Fig. 1). In this article, it was listed as one of 9 indications for the operation of "internal anal sphincterotomy," first described in 1951 (2). This particular abscess was cured by complete division of the internal anal sphincter over the abscess center. At this time the significance of this apparently rare abscess was not yet fully appreciated. Subsequently, it was recognized more frequently and this fact led to an article published in 1956 (4), dealing in detail with this pathologic entity. It was here named "the high intermuscular abscess."

THE HIGH INTERMUSCULAR ANORECTAL FISTULOUS ABSCESS

This abscess occurs much more commonly in the male between the ages of 40 to 55 years. Its onset is usually relatively mild, giving rise to a dull ache, heaviness, and fullness in the rectum. With progressive development, the symptoms become more acute. A continuous, deep and severe throbbing pain is present; sitting is difficult, and defecation becomes painful. Pyrexia and general malaise are present. These latter symptoms take 5 to 10 days to develop. A virulent infection may proceed with far greater rapidity.

The diagnosis is easily made in the earlier stages when digital examination of the rectum reveals a rounded fluctuant mass, about the size of a walnut, situated immediately above the levator shelf and generally in the posterior quadrant. Pressure on the swelling aggravates the pain. The corresponding anterior abscess, at this stage, is much less distinct owing to the absence of the levator shelf.

The abscess had expanded into the lax tissues of the rectum between the circular and longitudinal muscles of its wall. The symptoms are thus relatively mild. Diagram b of Figure 2 depicts this feature. As the main body of the abscess develops deep to the rigid internal anal sphincter it pushes the external sphincter muscle outward, and bidigital per rectum palpation now gives the impression of a large deep postanal abscess. This is shown in diagram c of Figure 2. In this advanced state, the distinct rounded mass above the levator shelf, in the rectum, is somewhat obscured and merges into a generalized brawny induration. The abscess finally appears in the subcutaneous tissue, lateral to the anal verge and distal to the lower border of the internal anal sphincter.

ETIOLOGY AND PATHOLOGY OF THE ANORECTAL INTERMUSCULAR SPACE INFECTION

The intermuscular space is shown in diagram c of Figure 2, expanded by the high intermuscular abscess. The medial wall is formed by the internal anal sphincter and its continuation above the circular muscle of the rectum. The lateral wall consists of the external anal sphincter with the fibromuscular conjoint longitudinal layer lying on its medial surface. The exact placing of the longitudinal muscle in the acute abscess is not demonstrable clinically. In a number of cases, the outer wall or floor of the abscess showed the external sphincter.

The localization of infection in this space merits consideration. The internal sphincter which forms the inner wall acts as an impermeable barrier to infection developed on

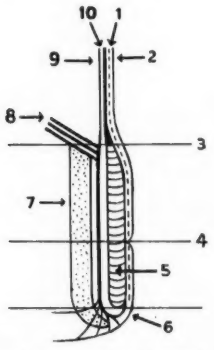

FIG. 1. Coronal section of anal canal. *1*, Submucosa; *2*, mucous membrane; *3*, anorectal line; *4*, dentate line; *5*, internal sphincter; *6*, anal intermuscular groove; *7*, external sphincter; *8*, puborectalis; *9*, longitudinal muscle of rectum; *10*, circular muscle of rectum.

its medial or internal surface. This conclusion is arrived at by the fact that the author has never experienced deep abscess formation following the severest forms of mucosal and submucosal inflammation above the dentate line in the anal canal, when complications develop, following submucous sclerosing injections for internal hemorrhoidal therapy. These complications vary from an inflammatory mass to abscess formation, necrosis, and even frank gangrene of the injected area. Yet, however gross this superficial infection may be, it never penetrates the internal sphincter barrier.

The vulnerability of the intermuscular space appears to lie in the crypts of Morgagni with their associated anal glands. These crypts, varying in numbers from 6 to 8, exist at the dentate or pectinate line and are best developed posteriorly. Opening into these crypts are the ducts of branched tubular gland-like structures, known as the anal or anal intramuscular glands. According to Bremer there are seldom more than 6 to 8 glands. The main ducts extend outward and usually downward and penetrate the internal sphincter where a flask-shaped swelling is usually encountered. Extending beyond this ampulla, there are several branches which continue through the internal sphincter and end blindly in the intramuscular connective tissue. Occasionally a tubule is seen piercing the longitudinal layer. Hill, Shryock, and Re-Bell state that the glands extending cephalad are usually simpler in structure—unbranched tubules—than those which extend caudad. They found that the glands usually only penetrated into the deeper portion of the submucosa and 3 out of 7 entered into the substance of the internal sphincter. In this series they found no glands deeper than that of the internal sphincter. Tucker and Hellwig have ably demonstrated these anal glands in microscopic studies of anal crypts excised at operation. As early as 1880, Hermann and Desfosses described glands of the terminal portion of the rectum and indicated their role in the causation of the abscess and the fistula.

Diagram a of Figure 2 shows 2 superimposed deep anal glands, cephalad and caudad, extending into the upper and lower portion of the intermuscular space via an anal crypt. The superficial anal gland, extending into the submucosa, is not depicted. The main concentration of glands is in the posterior quadrant of the anal canal. Anterior glands are far less common and true lateral ones, the rarest. This applies equally to the crypts. The deep proximally directed gland, which when infected gives rise to the high intermuscular abscess, occurs much less frequently than the distally directed deep gland. It is of simple structure and its upward direction also tends to prevent regurgitation of infected fluid. These factors tend to explain the relative infrequency of the high abscess as compared with lower intermuscular space infection.

The "low intermuscular abscess" results from infection of a deep caudally directed gland. This is the most common fistulous abscess and also generally occurs in the posterior quadrant. This abscess is shown in diagram d of Figure 2. It was thus named in a previous article (4).

The superficial anal glands, compared to the deep ones, are less liable to cause abscess formation, because the infected gland

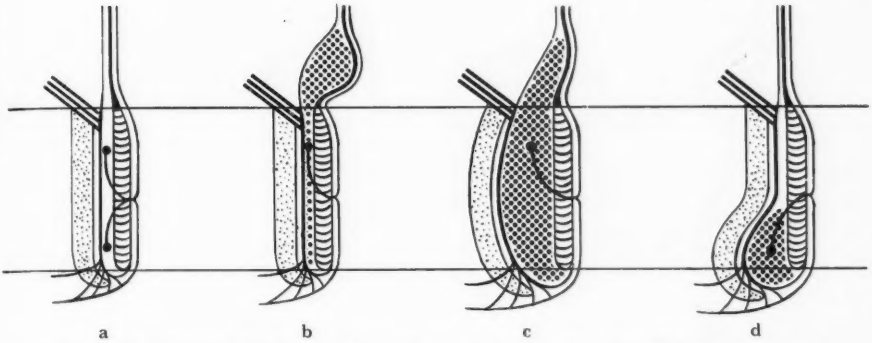

FIG. 2. The intermuscular anorectal fistulous abscess. a, Composite view of deep cephalad and caudad anal gland terminating in the intermuscular space. b, Early high classical intermuscular abscess. c, Fully developed high abscess pointing subcutaneously. d, Low intermuscular abscess is illustrated.

often has sufficient drainage via the crypt to allow of resolution.

A clinical finding, which strongly supports the cryptoglandular origin of the anorectal fistulous abscess, is borne out by the fact that seldom is the internal orifice of a fistula found anywhere else than in the vicinity of the cryptal mouths.

DISCUSSION

The high intermuscular abscess, situated deep to the internal sphincter and occupying the intermuscular space, is universally described and diagrammatically represented as the "submucous abscess." A true submucous abscess, a very superficial lesion, resolves spontaneously and does not permit of surgical intervention. The failure to recognize the intermuscular space abscess is responsible for much of the present day unsatisfactory treatment of the anorectal fistulous abscess. The high space abscess, when fully developed and appearing subcutaneously in the posterior quadrant is mistaken for a deep postanal abscess. This mistake results in formidable incorrect surgery whereas the correct diagnosis requires only the simple surgical procedure of total internal anal sphincterotomy over the central axis of the abscess in order to bring about a cure.

The intermuscular space bears the brunt of anorectal infective processes because the deep anal glands terminate there. It, consequently, also is the breeding ground of the more complicated fistulas. The author thus subscribes to the intermuscular space as the key to the surgery of this complex subject.

The term fistulous abscess is used because the two conditions are dissociable. The surgeon looks upon the abscess as different from the fistula whereas they are identical except in degree. The abscess represents the acute stage of the infective process whereas the fistula represents the chronic. When a fistulous abscess ruptures spontaneously, it becomes a fistula. Similarly, when a surgeon drains or deals ineffectually with such an abscess, a fistula results. The logical rationale, when possible, would be to effect a cure of both the abscess and the fistula in the combined stage. The term anorectal fistulous abscess should be used to stress the common parentage and pathology of this lesion.

The two following composite diagrams, a and b of Figure 3, are comparative and show clearly the distinction between the author's new concept and the generally accepted view of the anorectal fistulous abscess.

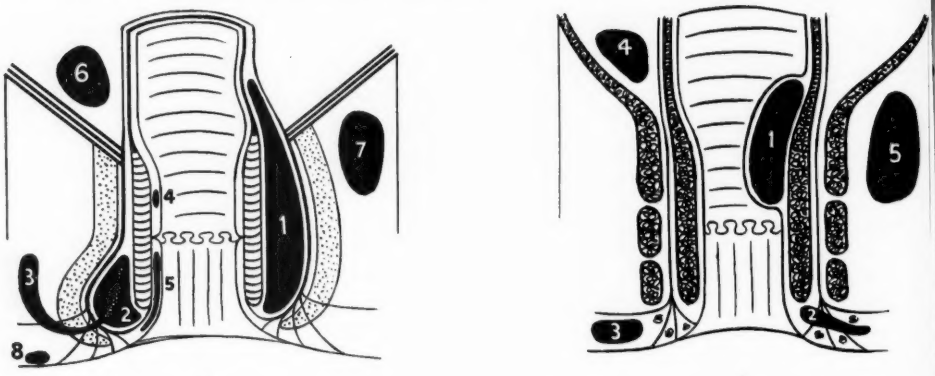

FIG. 3. Composite and comparative diagrams of the acute anorectal fistulous abscess. a, The new concept: *1*, high intermuscular fistulous abscess; *2*, low intermuscular fistulous abscess; *3*, intermuscular ischiorectal fistulous abscess (horse shoe lesion); *4*, submucous nonfistulous abscess; *5*, mucocutaneous fistulous abscess; *6*, pelvirectal abscess, nonanorectal; *7*, ischiorectal fistulous abscess; *8*, subcutaneous fistulous abscess. b, The currently held concept: *1*, submucous abscess; *2*, perianal abscess; *3*, subcutaneous abscess; *4*, pelvirectal abscess; *5*, ischiorectal abscess.

CONCLUSION

By attributing to the anal intermuscular space the leading role in the formation of the anorectal fistulous abscess, the old description and classification becomes untenable. The surgical approach to the intermuscular space is by division of the internal sphincter, an intra-anal procedure, whereas the abscess arising external to the anorectum is approached by an extra-anal operation. The suggested simple classification is based on this aspect with the exception of one combined type.

The classification of the anorectal fistulous abscess is as follows: Internal—high intermuscular; low intermuscular; mucocutaneous. External—ischiorectal; subcutaneous. Internoexternal—intermuscular ischiorectal.

The true submucous abscess arising above the dentate line in the anal submucous space, resulting from infected injections, trauma, or infective hematomas, resolves spontaneously and does not form a fistula. It is thus omitted from this classification. The pelvirectal abscess, secondary to pelviabdominal disease, is primarily not an anorectal condition and is also not included in the classification. These are both shown in the diagrammatic representation for comparison with the old classification.

The high and low intermuscular abscess arises from deep anal gland infection. The mucocutaneous abscess originates from a superficial anal gland and occupies the corresponding space below the dentate line.

The ischiorectal abscess is a lymphatic or blood-borne infection commencing in the lax fatty tissue of the apex of the fossa. The subcutaneous abscess occurs in the perianus. It is due to local tegumentary disease or to infection deep to the sentinel pile of a chronic anal fissure.

The intermuscular ischiorectal fistulous abscess develops from an extension of a low intermuscular abscess through its outer wall into both the subcutaneous space and the outer portion of the ischiorectal fossa. It arises from a posteriorly situated deep anal gland. This abscess is the so-called horseshoe type. When the origin is postcentral, the fistulous abscess often spreads later to the opposite side giving the double horseshoe pattern.

The frequency of the anorectal fistulous abscess in the author's practice is as follows:

high intermuscular, 10 per cent; low intermuscular, 81 per cent; mucocutaneous, 2 per cent; ischiorectal, 2 per cent; subcutaneous, 1 per cent; intermuscular ischiorectal, 4 per cent.

The diagram in Figure 4 represents the chronic or fistulous stage of the acute fistulous abscess.

With the evacuation of the main body of the abscess, after spontaneous rupture or simple drainage, shrinkage proceeds till finally a residual chronic granulomatous fistulous tract is left. The ensuing fistula bears the same name as its original parent abscess.

In Figure 4, the internal and interno-external group of fistulous abscesses each show 2 arrow marks, except for the high intermuscular one which has 3. The outer arrow represents the point of external or subcutaneous rupture, or external sinus of the ensuing fistula. The internal arrows with the exception of the superior arrow of the high intermuscular lesion, all point to the cryptal area of origin. Rupture occurs less often internally as the only point of drainage, in contrast to the external one. Discharge may proceed through the patent crypt from whose gland the original infection arose. This internal sinus, in the old standing fistula, is more often closed and the upper internal point of origin is a blind intermuscular pocket which may be well above the cryptal area.

According to this classification, 97 per cent of the fistulas have an internal cryptoglandular origin. The key to their radical cure lies, therefore, in dealing adequately with this area. The superficial low intermuscular fistula tends to encroach on the deeper type of mucocutaneous fistula where the tract, passing from the crypt to the skin, may traverse the lowest fibers of the internal sphincter as well as the subcutaneous fibers of the external sphincter.

Like the abscess, the majority of fistulas (over 90 per cent) occur in the posterior quadrant of the anal canal because this area is the site of election for the crypts with their

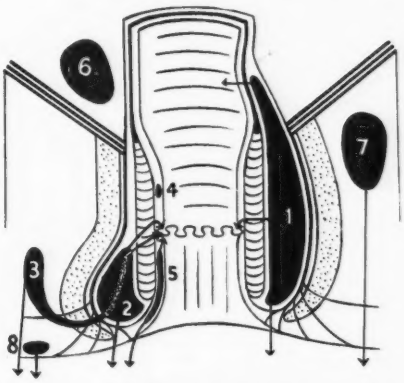

FIG. 4. The chronic anorectal fistulous abscess or anal fistula. The arrows represent the point of rupture and also the internal and external sinus of the resultant fistulas. *1*, High intermuscular fistula or chronic fistulous abscess. *2*, Low intermuscular fistula or chronic fistulous abscess. *3*, Intermuscular ischiorectal fistula or chronic fistulous abscess (horse shoe lesion). *4*, Submucous nonfistulous abscess. *5*, Mucocutaneous fistula or chronic fistulous abscess. *6*, Pelvirectal abscess, non-anorectal. *7*, Ischiorectal fistula or chronic fistulous abscess. *8*, Subcutaneous fistula or chronic fistulous abscess.

associated anal glands. The external group of fistulas, arising locally, account for a small percentage of the total. Here there is only an external sinus as indicated by a single arrow in the diagram.

An anterior fistulous abscess which warrants special mention has its external sinus at the base of the scrotum and generally to the left of the median raphe. It is of cryptoglandular origin forming either a low intermuscular or mucocutaneous type of fistula.

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THE EFFECT UPON THE HYPOPHYSIS OF RADIOACTIVE YTTRIUM

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EIGHT SURGICAL REMOVALS of the hypophysis were performed at the University of Chicago Clinics between March 1953 and September 1954 in an attempt to control advanced metastatic disease from various sites. The long term effects were not convincing, and the surgical morbidity and mortality left a great deal to be desired. The complications were numerous, and the autopsies revealed fragments of residual pituitary tissue.

Rasmussen set out to develop a more successful technique of ablation. He and his associates proposed destruction of the gland by the use of radioactive yttrium 90 pellets, placed directly in the hypophysis. The new procedure was designed to lessen surgical time, to reduce morbidity and complications, and to produce more complete, if not total, destruction of the gland.

RADIATION

Rough estimation of dosimetry, using photographic film, and extensive animal experimentation to determine the radiosensitivity of the hypophysis and parasellar structures preceded clinical use of radioactive yttrium.

Photographic film in a lucite phantom was simultaneously exposed to uranium oxide beta radiation and to radioactive yttrium pellets, and the effect of the yttrium measured by means of a densimeter, against the known effect of uranium oxide. In this fashion the isodose curves around a standard pellet were determined according to the method of Harper and associates (See Fig. 1—isodose curves).

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Similar pellets were then placed in the brains of monkeys, and the amount of radiation required for necrosis was determined for the pituitary and surrounding structures. The results (Table I) showed that the hypophysis was most resistant. The destruction was found to extend from 4 to 8 millimeters from the pellet, depending on the activity. It was estimated that 4 one millicurie pellets, properly placed, should totally destroy the pituitary without deleterious effects to the surrounding nerves and hypothalamus. In practice, however, it was found that the pellets could not be constantly placed in the desired distribution. Therefore, a larger number of pellets, with less individual activity, permitted a better distribution and more complete destruction than proved to be otherwise obtainable. The total quantity of isotope has been increased to 12 millicuries divided among 16 sources.

HISTOLOGIC OBSERVATIONS

There are 19 pituitary specimens radiated with varying quantities of isotopes with a wide spread of exposure time. The total millicurie dosages in this group vary from 1.3 to 6.5, and the time intervals extend from 20 hours to 16 months.

Technique. At autopsy, the entire bony sella has been removed en bloc and placed in formalin. If death has occurred within 1 month after placement of the pellets, the specimen has been set aside for radiation decay.

The pituitary has then been dissected out of the sella, and with the capsule kept in place, the beads have been gently teased

TABLE I.—RADIATION DOSAGE REQUIRED TO PRODUCE NECROSIS DOSAGE, REP

Anterior lobe of hypophysis	110,000 to 190,000
Hypothalamus	60,000 to 120,000
Optic chiasm or tract	60,000 to 140,000
Oculomotor nerve	30,000 to 60,000

out of the gland with a needle. Removal of the pellets is necessary for the protection of the microtome blades.

The gland has then been imbedded in paraffin, with the attempt to place it in the anatomic position, with the stalk up. Serial sections have then been prepared, from the inferior surface upward, at 10 microns' thickness. Every fortieth section has been mounted and routinely stained with hematoxylin and phloxine.

For evaluation of the percentage of destruction, the whole section has been projected on a glass plate at 10 power magnification. A direct outline of the entire gland has been traced on paper and the "normal" appearing area, drawn within the total area. The residual pituitary tissue stands out because of its retained stainability and the prominence of the nuclei. This preserved area has been checked with high power magnification to make certain that it conforms to the gross drawing. The areas of the entire gland and of the residual pituitary tissue have been estimated by planimetric measurement, and the percentage destruction has been easily calculated.

The possibility that embryonic rests might be contained in the tissues lying between the roof of the pharynx and the floor of the sella turcica has only recently been entertained and has not been eliminated in the cases under present consideration.

Dynamic pathology. By comparing the microscopic pictures of varying duration exposures, it is possible to give a progressive account of the necrotizing effect of the locally placed radioactive yttrium.

Within the first 24 hours, the areas adjacent to the individual pellets reveal acute hemorrhage, with disruption and necrosis of the tissue because of pellet placement. There is evidence of early vascular thrombosis, leucocyte infiltration, and marked edema (Fig. 2).

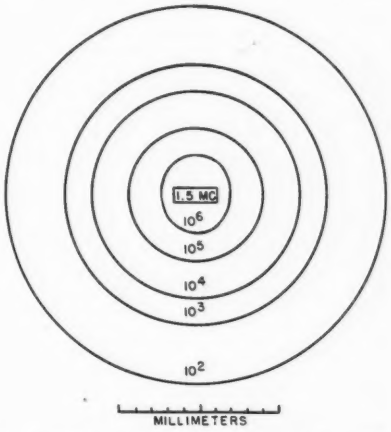

FIG. 1. Isodose curves (total dose in rep) around a 1.5 micron Y^{90} pellet in a lucite phantom.

All of the pituitary cells are swollen, show loss of stainability, and have clumped, pyknotic nuclei. It is not possible to postulate radiation effects at this time because prolonged agonal periods produce this type of change in the pituitary gland. The chromophobe cells show budding and bizarre, large nuclei in response to the acute damage.

At 5 days the general interstitial edema persists, recent hemorrhage is seen, and the

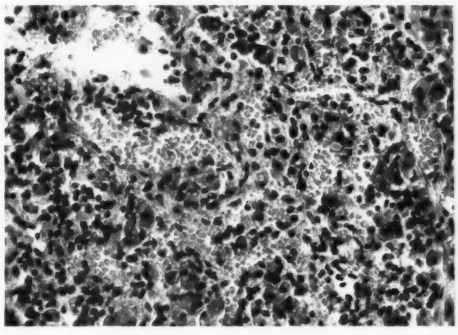

FIG. 2. Twenty hour survival. Section from area of pellet placement, showing hemorrhagic infiltration presumably mechanical in origin. The pituitary cells show swelling, and there is early clumping of chromatin.

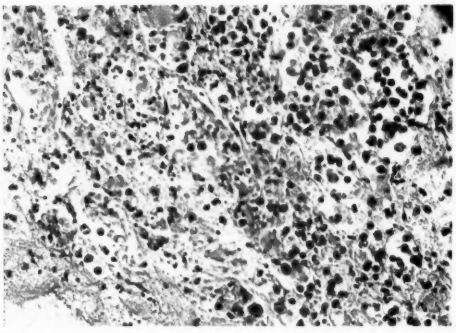

FIG. 3. Five day survival. The area is edematous and the pituitary cell clusters are disrupted. Near the pellet area dissolution of nuclei and of cell membranes may be seen.

phagocytes contain hemosiderin. The leucocytes are mostly round cells. The fibrous septa are separated, and the pituitary clusters are broken into individual cells (Fig. 3).

The zone of profound radiation effect has a fairly prominent border. Centrally, there is complete necrosis with loss of structure, and only ghost cells and debris remain. The next layer peripherally shows pyknotic, fragmented nuclei with loss of cytoplasm. Most of the vessels in the radiation zone are thrombosed except for a few at the periphery.

In the residual tissue the cells have clumped chromatin in small nuclei, and hazy, swollen cell membranes (Fig. 4).

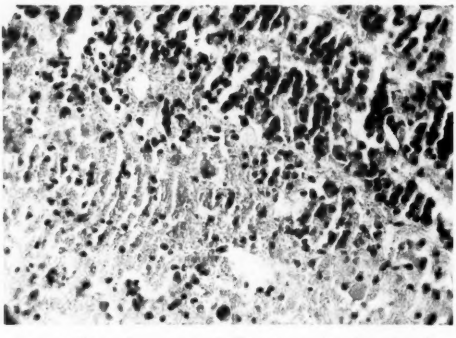

FIG. 4. Nine day survival. The sharp border of radiation necrosis is clearly demonstrated. Peripheral to the border the preserved cells are obviously profoundly altered.

From 9 days on, the border of radiation necrosis is sharply defined; but degenerative changes continue for 2 months, and in the final stage of dissolution only debris remains. Irregularly scattered throughout the residual tissue are numbers of cells showing decreased stainability, indefinite cell membranes, and pyknotic nuclei. These changes may well be independent of irradiation and are probably the reflection of the catabolic terminal state of patients dying from metastatic disease (Fig. 5).

There seems to be no morphologic difference in cell type radiosensitivity, as reflected in the later stages in a fairly normal ratio of basophils to eosinophils. The chromophobes are present in varying numbers, but all with uniform vesicular nuclei. There are no budding or bizarre nuclei to indicate hyperplastic proliferation.

The reparative process seems delayed for fibroblastic activity and vascular endothelial proliferation are not seen until 15 days. They begin on the border of the necrotic zone.

The edema resolves slowly and with the increase and contraction of the fibrous septa, the pituitary cells are reconstituted in clusters, but without the usual acinar or cord arrangement. There are only rare, isolated spots in which the original conformation is retained.

Phagocytosis and round cell infiltration in the debris persist for periods up to 2 months but are rarely seen in the active area thereafter, although they are present in minimal amounts on the fringe of the necrosis for longer periods of time (Fig. 6).

Therefore, the end stage shows a totally destroyed area that contains only debris within the necrotizing radiation zone. There are no nuclei to indicate living cells of any type. This destruction includes the capsule if it is within the range of critical radiation. The border of necrosis is a zone of approximately 5 to 10 cell layers, or less than 1 millimeter. This is mostly fibrous tissue forming a pseudocapsule with small clusters of pituitary cells enmeshed. Occa-

sional phagocytes containing debris are seen here. The residual pituitary tissue is peripheral and shows increased fibrous septa and an increased number of enlarged vascular channels. The cells themselves, both eosinophilic and basophilic, show a constant, chronic alteration in that they are shrunken in size, with reduced cytoplasm and small nucleus with dense, clumped, compact chromatin. They show good stainability and are obviously viable. Their arrangement within the clusters is upset because there are few acini or cords. The basophil to eosinophil ratio is probably normal.

Usually there is no posterior lobe tissue remaining, but we believe that this is due to the ease and frequency of pellet placement in this area, rather then to increased cell susceptibility. In those sections with residual posterior lobe cells there is a similar chronic alteration in the cells with reduced cytoplasm and clumped chromatin.

The only variations from this pattern were the occasional pituitary glands that had a small area of recent hemorrhage or vascular thrombosis. These processes were usually in the residual area so that they were easy to differentiate from any radiation effect. The area surrounding the acute necrosis showed new stages of degeneration, with pyknosis, ghost cell formation, and new round cell infiltration and phagocytosis. The cause of these spontaneous hemorrhages and thromboses is not obvious on the slides nor in the clinical record.

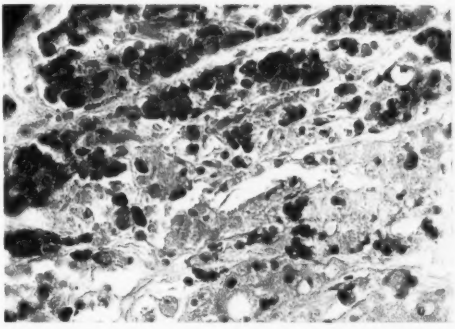

FIG. 5. Thirty day survival. Reconstitution of pituitary cells in groups devoid of usual acinar arrangement. Phagocytosis and round cell infiltration may still be seen at the edge of the necrotic area.

DISCUSSION

There remain many unsolved problems in the application of hypophysectomy to the treatment of metastatic cancer. It appears from the many reports of beneficial effects, that this form of therapy has at least a temporary place in our armamentarium. The present article presents an effort to solve one problem, that of finding the best technical method of pituitary destruction.

The clinical endocrinologic tests for pituitary function are not satisfactory. They are inferential and are based on the function of the secondary or target glands. Nor can we determine in our cases, with present histologic methods, the functional status of the residual pituitary tissue. We believe that most of the remaining cells, though viable, have been chronically altered, as evidenced by their shrunken size and small nuclei. At the border of the necrotic lesion the radiation dosage is about 200,000 rep. Two millimeters peripheral the dosage is about 20,000 rep, so that most residual cells have been very heavily irradiated. Significant questions are whether these cells are altered functionally, and whether yttrium radiation

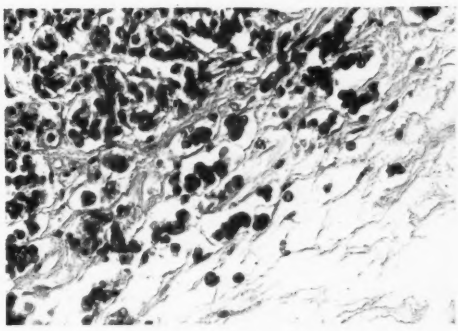

FIG. 6. Sixteen month survival. Shrunken pituitary cells with reduced cytoplasm and small dense nuclei at the border of zone of necrosis in which, at this stage, there are no living cells of any type.

can totally suppress function without corresponding total morphologic necrosis.

Although clinical data are not germane to this discussion, a correlation of presumed gland function, of its estimated effect on metastatic tissue, and of the pathologic picture of the locally irradiated pituitary gland seems allowable and desirable. In 19 autopsy specimens from our operative series of 43 cases, up to May 1, 1957, none of our slides have shown 100 per cent destruction. It seems safe to assume that very few, if any, of the still living patients have 100 per cent necrosis. Despite this fact, many of these patients have shown test evidence of reduced pituitary function. In 4 cases of the 43 there is good evidence of healing of metastatic lesions, and in 4 more of stabilized metastases. Does this finding suggest that there is total arrest of pituitary function with viable, but altered, pituitary tissue left? Or may beneficial clinical response be seen in certain susceptible metastases when only a reduced pituitary function is achieved?

SUMMARY

Radioactive yttrium pellets, placed in the pituitary gland, effect total necrosis in a diameter of approximately 4 to 8 millimeters, depending on the activity of the pellet. Multiple pellet placement produces coalescent necrosis with a sharp border. There is a fibrous pseudocapsule formed in which a few pituitary cells become enmeshed. Tissue peripheral to the border shows chronic alteration, characterized by shrunken cells with small nuclei and clumped chromatin. The functional status of this tissue remains to be determined.

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THE EFFECT OF SKIN TRANSPLANTS ON SERUM PROTEINS IN EXPERIMENTAL ANIMALS

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THE ACCEPTANCE of homologous skin transplants in the human host devoid of gamma globulin is indicative of the importance of this protein fraction. Alterations in the concentrations of serum proteins, particularly gamma globulin, may associate an immunologic mechanism with the acceptance or rejection of a homograft.

To elucidate further such a role of gamma globulin, as well as other serum proteins, the changes in serum protein concentrations were determined in mice, guinea pigs, and rabbits following autogenous and homologous skin transplants.

MATERIALS AND METHODS

Full thickness skin grafts approximately 1 square centimeter in area obtained from mice, guinea pigs, and rabbits were transplanted on the surface or subcutaneously. The surface grafts were sutured with No. 0000 black silk into a patterned surgical defect. The subcutaneous grafts were folded with raw surface out and inserted through a linear incision which was sutured over the graft. Autologous and homologous grafts were transplanted by each technique to 3 species of animals. For each type of transplant there were 140 CFW recipient mice, 13 to 15 guinea pigs, and 8 to 10 rabbits. The animals were observed for 21 days, and serum was collected every third day. Each serum sample to be used for electrophoretic studies consisted of a pool from 20 mice or 2 guinea pigs chosen at random. Serum samples from the rabbits consisted in every instance of a pool from all the rabbits used for each type of transplant; serum was collected by cardiac puncture and stored at −20 degrees C.

Electrophoretic analyses were made with filter paper No. 300-028 in a Model R Durrum type cell. Veronal buffer (*p*H 8.6 and ionic strength 0.075) was employed in the analyses. Separations were made at 5 milliamperes for 16 hours at room temperature (68 to 70 degrees F.). The bromophenol blue-acetic acid method was used for staining. Stained patterns were scanned with an Analytrol. Each serum was run in triplicate.

RESULTS

Preliminary studies on electrophoretic analyses of serum. Table I contains data from an experiment demonstrating the feasibility of utilizing pooled samples of serum. Pooled samples of serum were used to conserve on materials and time. Protein analysis by the electrophoretic procedure described was performed on serum from 6 individual mice. The results from a pool of serum consisting of equivalent amounts of serum from the same 6 mice were nearly identical to averages computed from the individual samples. Data are also presented in Table I to demonstrate the variation in results for each protein concentration when an electrophoretic analysis was performed on the same serum samples 4 times. Because of variations inherent to the experimental procedures each serum was analyzed in triplicate, and the values for normal serums of each species were obtained from 6 pools of serum, in each instance from 6 different animals.

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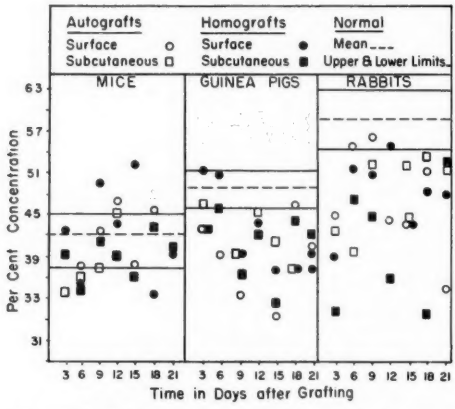

FIG. 1. Relative concentrations of albumin in serum of mice, guinea pigs, and rabbits with skin grafts.

Table II contains data obtained from serum samples which had been subjected to freezing and thawing as many as 5 times. Serums were frozen by placing in a deep freeze with a temperature of −20 degrees C. Thawing was done by placing the serum at room temperature (68 to 70 degrees F.). Thus, the serum samples were subjected to relatively slow freezing and thawing procedures. As can be seen from the data in Table II, the variations in results cannot be correlated with the number of times a serum was frozen and subsequently thawed. Consequently, fresh samples of serum were not necessary for electrophoretic analysis.

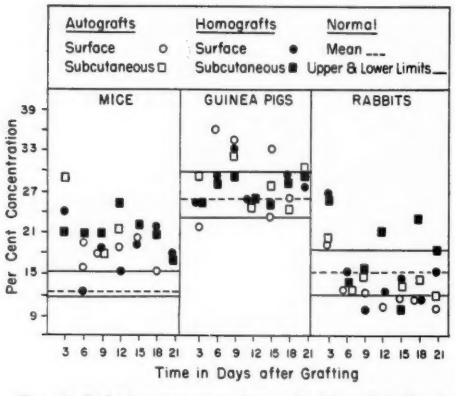

FIG. 2. Relative concentrations of alpha globulin in serum of mice, guinea pigs, and rabbits with skin grafts.

Studies on the effects of skin grafts on serum proteins. Three species of animals—mice, guinea pigs, and rabbits—were used to study the effect of skin grafts on the electrophoretic patterns of serum globulins and albumin. Comparative studies were made with autologous and homologous grafts which were transferred to recipients by two methods: surface and subcutaneous. The variations in experimental methods permitted comparisons between: (1) long lasting grafts (subcutaneous homografts) with those remaining on the host for a relatively short time (surface homografts) as well as (2) skin grafts which were placed in a natural position (surface autografts) with those in an area expected to produce a reaction due to placement in an unnatural position (subcutaneous autografts).

The maximum and minimum concentrations (relative) of the various proteins in each species are represented in the figures as horizontal solid lines; the mean values are depicted as broken horizontal lines.

As can be seen in Figure 1, the relative concentrations of albumin remained unchanged in mice but there was a decrease for this protein in guinea pigs and rabbits. The concentration of alpha globulin shown in Figure 2 was increased for mice but remained constant for the other two species. Figure 3 reveals that the beta globulin decreased in concentration in mice but remained unchanged in guinea pigs and rabbits.

Marked changes in concentration of gamma globulin were observed in guinea pigs and rabbits (Fig. 4). In these species the gamma globulin showed an increased concentration which became more pronounced toward the end of the 21 day observation period. In mice this protein remained relatively unchanged.

When considering the effects on the protein concentration in relation to a specific type of skin graft, it becomes apparent

that no one type of skin graft, by either of the two grafting techniques, was responsible for the results obtained. It is of interest that the protein fractions which complement each other by opposite changes in concentration are different in mice and the other two species. In mice the increase in the alpha globulin fraction occurred concomitantly with a substantial decrease in beta globulin and a slight one in gamma globulin. However, in both guinea pigs and rabbits an increased concentration of gamma globulin was consistent with a decrease in albumin. These data suggest a different mechanism of response to the experimental procedures in mice when compared with guinea pigs and rabbits. Total protein determinations were done on most of the sera which had been analyzed electrophoretically. There were no appreciable changes in concentration which could be correlated with alterations in the relative concentrations of individual protein fractions.

Histologic sections, stained with hematoxylin and eosin, were made of all skin grafts 3 through 21 days following the grafting procedure. All homografts in mice were dead by the seventh or eighth day and in rabbits and guinea pigs by the ninth day. For autografts there was over 90 per cent acceptance and viability. The subcutaneous implants showed cystic formation with cellular debris and the subcutaneous homografts showed more infiltration with lymphocytes and polymorphonuclear neutrophiles.

TABLE I.—COMPARISON OF PROTEIN CONCENTRATIONS IN INDIVIDUAL AND POOLED MOUSE SERUM SAMPLES

	Serum proteins			
Serum samples	*Albumin*	*Alpha*	*Beta*	*Gamma*
Individual samples				
Mouse 1	36.9	18.8	32.1	12.2
Mouse 2	33.7	10.0	45.0	11.3
Mouse 3	32.2	17.8	31.5	18.5
Mouse 4	41.7	15.5	22.2	20.6
Mouse 5	42.0	16.2	32.0	9.8
Mouse 6	44.8	21.7	21.2	12.3
Computed average	38.6	16.6	30.6	14.2
Pool of Nos. 1-6:				
Sample 1	38.0	13.2	33.3	15.5
Sample 2	40.7	15.2	26.1	17.8
Sample 3	44.6	13.3	28.7	13.3
Sample 4	45.2	12.6	29.1	13.0
Computed average	42.1	13.6	29.3	14.9

DISCUSSION

Disturbed protein equilibrium following injury has been studied in human beings and animals. Cuthbertson and Thompsett showed a decreased albumin and an increased globulin fraction following injury. In their method none of the globulins, however, were studied individually.

Hoch-Ligeti and associates employing paper strip electrophoresis studied the serum proteins of 45 patients undergoing surgery. They observed a significant decrease in albumin. The alpha$_1$ and alpha$_2$ globulins were similarly decreased in one-third of the cases during a 24 hour postoperative period. These changes were present in 80 per cent of cases during the next 4 days. Thereafter the serum components returned to preoperative levels. Total serum protein and hematocrit determinations did not show any significant variation in the early postoperative periods. An increased concentration albumin together with a decreased globulin level prior to operation may reflect a protein depletion due to a patient's respective disease. It has been shown that a negative nitrogen balance does not occur after injury in patients who have little nitrogen reserve due to malnourishment or

TABLE II.—EFFECT OF FREEZING AND THAWING ON SERUM PROTEINS

Times frozen	*Rabbit serum*				*Guinea pig serum*				*Mouse serum*			
	alb.	α	β	γ	alb.	α	β	γ	alb.	α	β	γ
0	63.0	18.0	12.6	6.4	46.1	29.0	15.2	9.7	45.9	13.5	23.7	16.9
1	56.0	13.2	23.9	6.9	52.0	23.3	14.4	10.3	39.1	13.3	30.2	17.4
2	62.4	13.5	11.2	12.9	46.0	27.0	16.4	10.6	46.0	13.5	26.7	14.8
3	55.0	19.0	18.3	7.7	49.2	25.2	17.2	8.4	33.9	16.6	32.9	16.6
4	56.9	11.7	17.2	12.8	52.0	26.7	12.2	9.1	41.1	9.5	28.9	20.5
5	61.2	12.2	15.8	10.7					42.8	7.5	29.9	19.8

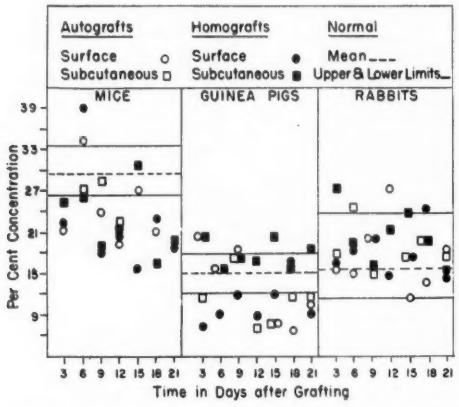

FIG. 3. Relative concentrations of beta globulin in serums of mice, guinea pigs, and rabbits with skin grafts.

protein depletion. The gradual increase of serum albumin during the early postoperative days is in agreement with the observation of Cuthbertson and Thompsett that the nitrogen excretion in the urine was not excessive immediately after operation and only after 3 or 4 days did it become considerable.

The mechanism of negative nitrogen balance is still unknown. It is thought that the direct destruction of tissues during operation is not the responsible factor. There are similarities in nitrogen metabolism and the adaptation syndrome of Selye.

The adrenocortical hormone of the pituitary and 11-oxycorticoids have produced negative nitrogen balance. A disturbance of the enzyme systems of the liver, those responsible for protein metabolism, may be responsible also for postoperative protein disturbances.

A disturbance in concentration of serum proteins has been reported in infections such as tuberculosis and hepatitis, in malignant neoplasms, arteriosclerosis, rheumatic heart disease, cirrhosis, and rheumatoid arthritis. The most consistent finding was a decrease in the serum albumin concentration, followed in descending order, by an elevation of alpha$_2$ globulin, gamma globulin, and beta globulin. Increased levels of albumin and decreased levels of serum globulins rarely occurred.

The rise in alpha$_2$ globulin was observed often in association with inflammatory and tissue destruction due to an increase in concentration of glycoproteins. Gamma globulin fraction was most frequently elevated in chronic infections, connective tissue disease, and certain liver diseases.

We have recently reported (5) the effects of cortisone and x-radiation on serum proteins in experimental animals. CFW mice were injected with 4 milligrams of cortisone or received 300 roentgens of total body irradiation. Both x-rays and cortisone produced a depressing effect on gamma globulin. There was no appreciable effect on the concentrations of albumin and alpha or beta globulin.

Plasma protein changes during the growth of sarcoma 180 in C57BL/6 mice were studied by Bernfield and Hamburger. The tumor growth significantly increased the alpha globulin fraction of the plasma and decreased the albumin. The authors suggested that the changes in alpha globulin were actually associated with the neoplastic growth.

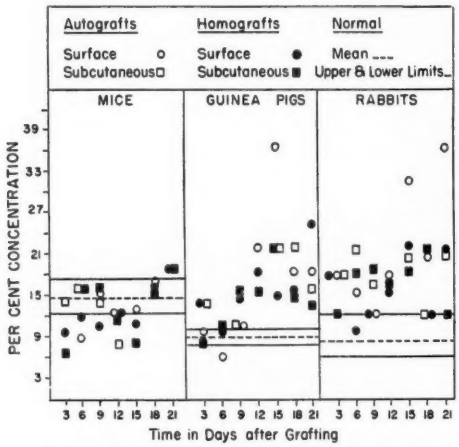

FIG. 4. Relative concentration of gamma globulin in serum of mice, guinea pigs, and rabbits with skin grafts.

The plasma protein fractions as studied in our experiments would indicate that the changes in protein concentrations are a reflection of stress or injury. The immune response does not seem to be implicated in the reflected changes of the protein fractions.

SUMMARY

The alteration in concentrations of albumin and alpha, beta, and gamma globulin of serum following experimental skin transplants is probably an expression of a stress or injury. Guinea pigs and rabbits showed essentially the same changes in the protein concentrations: increased concentrations of gamma globulin with a decrease in albumin. In mice the relative concentration of alpha globulin was increased; the beta globulin fraction was decreased.

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APPENDICITIS IN THE OLDER PATIENT

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THE MORTALITY RATE of appendicitis is often thought of as being insignificant, but actually in the elderly and the very young this disease still carries a definite hazard. Recently, the cases of appendectomy at Ancker Hospital, a city-county hospital, were reviewed and a high fatality rate was found among the older patients. It was noted that 85 per cent of the deaths occurred in patients 45 years of age or older. The significance of this fact and the circumstances surrounding it form the basis of this report.

CLINICAL MATERIAL

During the 9 years between January 1947 and January 1956, 563 appendectomies were performed, exclusive of those which were performed as an incidental procedure to other abdominal surgery.

Age and mortality rate. The patients were divided into two groups in order to analyze the importance of age: (a) patients under 45 years of age, and (b) patients 45 years of age or older. The first group consisted of 497 persons, whereas the later group consisted of 66 persons. A study of these two groups revealed that, although those in the older age group comprised only 11.7 per cent of the series, 85 per cent of the deaths occurred among these patients. The mortality rate in the older age group was 9.9 per cent compared to 0.2 per cent in the younger group. The over-all mortality was 1.24 per cent.

The impression was gained in the wards that many of these older patients had had symptoms for an exceptionally long period of time, and this impression has been confirmed by our review. We found that 22 per cent of those in the older age group had had symptoms for more than 96 hours before admission to the hospital. Among the younger patients only 7.2 per cent had delayed this long before admission. The average duration of symptoms before hospital admission among those of the older group was 60.5 hours, whereas it was 13.6 hours in the younger group.

The time interval between hospital admission and surgery was identical in both groups. In only 10 per cent of each group was operation delayed for more than 24 hours by the medical staff.

Pathology of surgical specimens. Pathologic examination of the surgical specimens showed that in the older age group 10.1 per cent of the appendixes were gangrenous or ruptured. On the other hand, only 3.7 per cent of the specimens in the younger group were gangrenous or ruptured. Thirty per cent of the patients who delayed more than 96 hours in seeking medical help had gangrenous or ruptured appendixes.

It was also found that 15.4 per cent of the specimens removed in the older group were normal, whereas 21.4 per cent of the specimens in the younger group were normal indicating that possibly the younger patients sought medical aid before gangrene could develop.

Two deaths in this series are classified as anesthetic deaths according to Beecher's criteria. One occurred in a 3 year old boy with an acute appendicitis and a severe case of chickenpox. He died in the operating room of anoxemia secondary to edema of the respiratory tract. This was the only death among those patients under 45 years of age.

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The other occurred in a 56 year old male who died in the operating room of cardiac arrest. He had had no previous cardiac disease. Pathologic examination of the appendix revealed chronic inflammation.

Acute cholecystitis in the postoperative period caused the death of 1 patient in this study. He was a 48 year old male who succumbed on the tenth postoperative day. Autopsy revealed a generalized peritonitis secondary to a gangrenous cholecystitis. The appendix which had been removed showed acute inflammation.

The remaining 4 deaths, all in the older age group, were the result of generalized peritonitis caused by gangrenous or ruptured appendixes. The ages of these patients at the time of death were 81, 70, 63, and 53 years. An average of 10 days elapsed between the time of surgery and the time of death in these cases. The mortality rate in gangrenous appendicitis was 11.7 per cent compared to 0.7 per cent in nongangrenous appendicitis. No deaths occurred among those patients whose appendixes were normal.

DISCUSSION

In this series the high death rate in the older patients is seemingly related to the long delay between the onset of the symptoms and the seeking of medical help. This delay allows the pathologic process to advance uncontrolled, which in turn results in a greater incidence of ruptured and gangrenous appendixes and secondary peritonitis. The older patient waited an average of 60.5 hours before seeking help, whereas the younger patients delayed only an average of 13.6 hours. Correspondingly, in the older age group the incidence of gangrenous specimens was 10.1 per cent, and in the younger group, only 3.7 per cent. The incidence of gangrenous specimens in all patients delaying treatment for more than 96 hours was 30 per cent.

Similarly, the incidence of normal specimens in the older patients was less than in the younger patients. Inasmuch as the time interval between hospitalization and surgery was identical in both groups, the difference in time between onset of symptoms and the seeking of medical help is of significance.

The rapidity with which infections spread in older patients has been recognized for many years. This fact may be due in part to the frequency of malnutrition, avitaminosis, anemia, and decreased blood volume. When such an elderly patient does present himself for medical care he must be treated as an emergency. As has been observed by Haug, emergency procedures in this type of patient carry an increased mortality rate.

The use of antibiotics is not a panacea in the treatment of elderly patients. Of the 6 deaths among the older patients, 5 were due to peritonitis, although all these patients received massive doses of broad spectra antibiotics.

As pointed out by Titchener and associates, the reason for delay on the part of the older patient is sometimes psychologic. Several of our patients expressed a desire to be left alone and allowed to die. This sort of feeling is commonly expressed by older patients beset with social and economic ills; a patient of this type is commonly seen at Ancker Hospital.

It is necessary that all physicians be more aware of the mortality rate associated with acute appendicitis in older patients. Physical findings in the older patients may be bizarre. Any delay in treatment is hazardous. Vigorous postoperative care is imperative. An educational program directed toward the patients in this age group most likely would be unsuccessful.

SUMMARY

1. A review was made of the 563 patients undergoing appendectomy at Ancker Hospital between 1947 and 1956. A comparison of results was made between patients 45 years of age or older and patients less than 45 years old.

2. The over-all mortality rate was 1.24 per cent. In patients 45 years of age or older, the mortality rate was 9.9 per cent

and in patients under 45 years of age the mortality rate was 0.2 per cent.

3. The incidence of gangrenous or ruptured appendixes in the older age group is twice that in the younger group.

4. The older patient delayed in seeking medical aid for an average of 60 hours after the onset of symptoms, whereas the younger patient delayed for an average of only 13 hours.

5. Generalized peritonitis was the main cause of death and is related to the high incidence of ruptured or gangrenous specimens which is in turn related to the delay in seeking medical help.

6. An awareness of these facts on the part of the physician may alter the mortality rate in the future.

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EDITORIALS

FETISHISM IN SURGERY

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SURGERY, especially in its operative aspect, has always had strong ritualistic overtones. This was particularly notable in earlier days when operative procedures were limited in number and scope and their performance demanded the greatest economy of time and movement. Speed and dexterity were the *sine qua non* of the successful operating surgeon, and the surgical apprentice copied slavishly each maneuver of his master. Many surgical technicians were famous for a particular operation or for special instruments, which were bequeathed as a legacy only to a favored few who attempted to preserve the proprietary character of the technique.

The advent of anesthesia abolished the major need for excessive speed in operating and permitted a more deliberate and considered approach in contrast to the headlong, inflexible routine of the preanesthetic era. Anesthesia also made possible more complex operations which on this account alone were less likely to be performed repeatedly in a slavishly identical way. A further step in the evolution of surgery away from a rigidly stylized, mechanical craft was the application of basic science to everyday management of the surgical patient. Indeed, we have come a long way toward that millennium envisaged by Harvey Cushing when he looked to the day that university authorities would appoint as professor of surgery a man with no hands.

Despite an occasional approximation to this acheirous surgical estate, there are still many instances in which the chief task of surgical management lies in the operative act. Many of the maneuvers we employ in such "routine" operations tend to be thoughtless and stereotyped. When diffuse surface bleeding occurs, for example, we still hear surgeons call for "a nice hot pack" as a mechanism for local hemostasis. Certainly such men are aware of the erythematous response to local heating of tissues. A moment's reflection suggests that the effect of local heat is to enhance bleeding, rather than to arrest it.

Willman has shown experimentally that when sponges moistened in saline solutions at 65 degrees C. are applied to skin graft donor sites in animals, the blood loss is greater than with application of similar sponges at room temperature or below. The difference in blood loss may not be important to the patient's welfare, especially in an era when it is sometimes considered simpler to transfuse than to bother with hemostasis. The point of interest here is not so much the saving of blood as the rational use of a physical modality in treatment. The heating of solutions for moistening sponges in modern operating rooms harks back to a day when it was considered essential that nothing should touch the exposed tissues unless it were at the precise temperature of the body. These early efforts to co-operate with the body's homeostatic mechanisms were laudable but we now recognize that localized cooling of tissues or even severe general bodily hypothermia is well tolerated and in certain circumstances beneficial.

As a result of attempts to avoid local cooling, we may raise the temperature of solutions so high as to burn the tissues, since temperatures as high as 65 degrees C. may be tolerated for 10 seconds or more by the rubber gloved hand. A nurse may handle sponges briefly at this temperature without being aware that the solution is anything but "warm." If the temperature of solutions is kept constant at 37 degrees C., we usually achieve this dubious caloric ideal by wasting the time of a circulating nurse who might better be occupied in more essential tasks. A rational and practical plan employs such solutions at toom temperature; avoiding the Scylla of scalding and the hypothetic Charybdis of shock due to cooling.

One could cite other instances of adherence to traditional practice long after the rational basis for such practice has disappeared. Consider the problem of silk and catgut. The use of fine sizes of silk as an integral part of meticulous hemostasis and careful handling of tissues was a major technical contribution of Halsted in the days when catgut was made only in large sizes with unsatisfactory standardization and inadequate bacteriologic controls. Now that catgut is safe and standardized, the use of extremely small sizes may call for greater delicacy in handling than with certain commonly used sizes of silk. Under these circumstances a surgeon trained in so-called silk technique may use catgut with due regard for Halstedian principles, while another may violate these principles even though he uses nothing but silk. Tissue can be strangulated as well with a heavy ligature of one material as it can with another material, and silk is not a fetish to ward off the evils of heavy handed operating.

A British surgeon well known as a trenchant and provocative writer once listed among the adverse factors affecting American surgery "the Halsted tradition." In view of Halsted's major influence in graduate education alone, one must differ with this appraisal after two decades of further consideration. However, our English critic was writing particularly of those who followed the details of Halsted's technique even though they had lost sight of the objective with which these details were introduced. In this criticism we must concur as well as in rejecting a slavish adherence to any other surgical tradition. At present the climate of opinion in America seems more favorable to the proposition that change necessarily connotes progress, which may be as unrewarding a position as the conviction that tradition must determine our surgical techniques. In technical matters as in broader concepts of surgery, we should make a fetish neither of change nor of tradition, but rather attempt to be guided by logic and by critical analysis of collected experience.

EXTRACORPOREAL CIRCULATION IN CARDIAC SURGERY

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DURING THE PAST FEW YEARS a spectacular new method for performing open cardiac operations was introduced which opened a vast and almost unexplored field for cardiac surgeons. In this relatively brief period it has been clearly demonstrated that mechanical devices can be used successfully to substitute temporarily for the function of the heart and lungs. Numerous investigators had already devoted much effort and study in the experimental laboratory to the development of a pump oxygenator system which would be safe and practical for human use. Gibbon's devoted efforts deserve greatest recognition during this preclinical period, but others including Dennis, Clark, Gollan, Bjork, Weslowski, and many more made important contributions. Although Gibbon first successfully used the mechanical heart-lung clinically in a case of atrial septal defect, Lillehei and his able co-workers, who used a method of cross circulation for cardiac bypass, convincingly demonstrated that life could be supported by artificial means while the heart and lungs were temporarily excluded from the circulation with an acceptably low mortality. Unquestionably their results in the first forty-odd patients operated upon by using a pump and a biologic oxygenator or lung of the donor provided the needed stimulus to break the barrier between the experimental laboratory and actual clinical application. Subsequently Kirklin and his group, using a modification of Gibbon's apparatus, demonstrated that a completely mechanical pump and oxygenator system was practical and provided sufficient time of open cardiac conditions in which to correct complicated congenital defects. Their carefully controlled studies on patients undergoing lengthy open cardiac procedures reassured even the most skeptical observer that the era of extracorporeal circulation had definitely arrived. Lillehei and DeWall perfected a simplified bubble diffusion type oxygenator and have operated upon more than 300 patients using cardiopulmonary bypass. Kirklin and his associates report more than 250 such operations. These techniques with certain modifications have been adopted in other centers, and we have operated upon 275 patients using cardiopulmonary bypass.

Recently, the Surgery Study Section of the United States Public Health Service and National Institutes of Health organized a conference on problems of extracorporeal circulation which provided an opportunity for active workers in this field to express their opinions regarding certain problems peculiar to this project and to compare results. Several types of pumping mechanism were described, and the requirements for an ideal pump were discussed. In general three types of oxygenator are in use including the vertical screen type, the membrane type, and the bubble diffusion type. Each method has apparently proved to be clinically successful, yet each has both theoretic and practical disadvantages. Bubble oxygenators are considered by many to be inferior and admittedly give poor results in laboratory animals, yet DeWall reported only 1 death in a consecutive series of 40 patients operated upon using this type of oxygenator, certainly an enviable record for any apparatus or method. Some advocates of the membrane and screen oxygenators reported not only equally good results in the clinical application of their oxygenators but in addition more satisfactory results in the laboratory than were obtainable with a bubble oxygenator.

Difference of opinion still exists regarding

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the optimum rate of flow during cardiopulmonary bypass. Kirklin has steadfastly recommended a so-called high flow rate approximately 2.3 liters per square meter body surface per minute or approximately 120 cubic centimeters per kilogram body weight per minute. Results of his own operations appear to justify completely his conviction, since in the last 51 cases of bypass only 1 patient succumbed. These results, however, are not significantly better than those of DeWall and Lillehei, who employed relatively low rates of flow 50 to 70 cubic centimeters per minute. Some factor or factors other than the natural adaptability and resistance of the human organism to surgical and physiologic insult must be present which explains the apparent success of the two techniques of perfusion. Perhaps the explanation of this apparent paradox lies partly in the varying degree of oxygenation of blood. Bubble diffusion oxygenators have a tendency to "supersaturate" the blood and may produce an oxygen tension as much as 5 times greater than for normal arterial blood which is approximately 100 millimeters of mercury. Using an oxygenator which produces an oxygen tension in the blood which is approximately normal for arterial blood, one could and should use rates of flow roughly that of the resting patient at basal conditions which to surgeons is considered "high flow." On the other hand, if the oxygenator produces an oxygen tension several times normal for arterial blood, a high flow rate may be harmful leading to bubble formation and possibly to the ill-defined state known as oxygen poisoning. Attempts to reduce or increase the rate of arterial blood flow without an appropriate alteration in oxygen tension presumably therefore could lead to undesired results. Not only must one consider the problem of adequate perfusion of oxygen into the tissues but also the elimination of the waste products of metabolism. Adequate flow, therefore, should provide for the oxygen needs and at the same time offer optimum conditions for carbon dioxide and lactic acid elimination. Such factors may account for conflicting reports on development of acidosis and other physiologic disturbances after bypass. Ultimately some agreement must be reached regarding estimated optimum flow rates during cardiopulmonary bypass. These estimates should take into consideration, however, the oxygen tension of the blood returned to the arterial system and possible metabolic needs of the tissues at the time of bypass.

Other important problems in this field are still unsolved. Circulation of blood through a mechanical circuit produces hematologic changes such as hemolysis, platelet destruction, defibrination, fibrinolysis, and denaturation of protein. Little is known about the effect of artificial perfusion on specific organs such as the brain, kidneys, liver, and lungs. Cardioplegic agents, particularly potassium citrate and acetyl choline, which are in use in many centers introduce another area for investigation to determine whether the advantages provided outweigh the possible harmful effects from delayed myocardial recovery. Prevention and control of cardiac conduction defects during and after operation are still a matter of serious concern since heart block remains one of the principal causes of death after such operations. Management of the patient with increased pulmonary vascular resistance also presents a continuing problem which is far from satisfactorily concluded. Many such problems will be solved as clinical experience accumulates with the assistance of carefully controlled experiments in the animal laboratory, and the safety of such operations will be steadily increased.

While most efforts are presently being directed toward increasing the capacity of the extracorporeal system in order to maintain the entire body in a homeostatic state during periods in which the function of the heart and lungs are excluded from the rest of the body, the future success of open cardiac surgery may depend upon reduction in the demands placed upon the pump oxygenator system. Minimal perfusion rates could probably be made to suffice by reduction in

metabolic requirements of the tissue through use of a metabolic blocking agent which has a reversible action on the oxidation processes in the cell. Such a drug should have a temporary action, a dependable antidote, and should produce no permanent cellular damage. Hypothermia could probably be utilized in several ways in conjunction with temporary extracorporeal circulation. Induced local tissue hypothermia to protect the vital organs of the body such as the central nervous system may be practical, and if the temperature of the blood stream were not altered appreciably, the cardiac complications of general body hypothermia could be avoided. Furthermore, minimal requirements for survival may be met by temporary perfusion of only the brain and perhaps the kidney and liver during the brief periods of open cardiac procedures. While most investigators strive to develop the ideal, self-regulated heart-lung apparatus, an equally strong effort should be made in the direction of simplification of the machinery and other paraphernalia. At present many of the methods of extracorporeal circulation could only be employed in large well equipped medical centers, and even there the techniques are often too complex to be safe and practical. Certainly reduction of the required volume of flow rates through the extracorporeal system should reduce the importance of certain complicating factors which now plague this project. Ultimately a practical and simple technique will emerge and open heart surgery should be available in all hospitals where closed cardiac surgery is being performed at present.

One fact should be recognized at this early stage in the development of open heart surgery, i.e., a surgeon who is technically adept, thoroughly familiar with cardiac pathology and physiology, and temperamentally suited for a demanding situation will probably be the deciding factor in the success of such procedures.

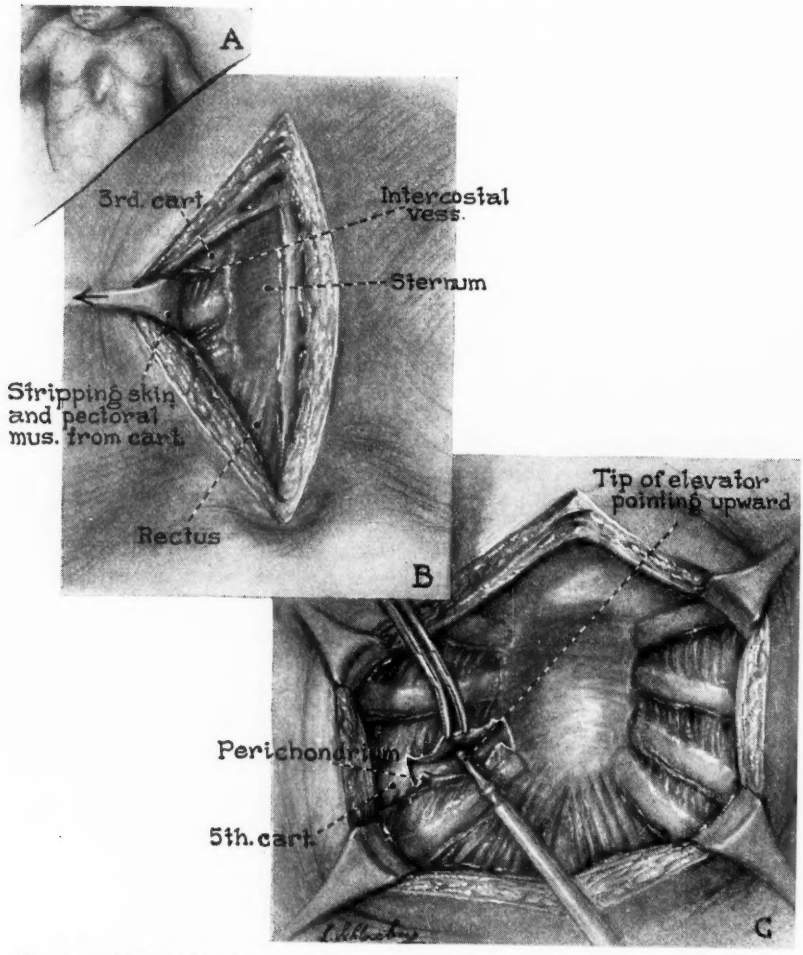

FIG. 1. A midline incision is employed from the manubrium to the epigastrium and a flap of skin, fat, and pectoralis major is reflected back on either side (B). The perforating vessels are brought into view and are clamped and divided as this is done. Longitudinal incisions are made in the perichondrium of the deformed cartilages with cross incisions at either end. The perichondrium is elevated with fine instruments aided by traction on the cut edge (C).

Operation for Correction of Pectus Excavatum.—Mark M Ravitch.

THE SURGEON AT WORK

OPERATION FOR CORRECTION OF PECTUS EXCAVATUM

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THE DEFORMITY known as pectus excavatum, funnel chest, and trichterbrust has been treated operatively for some 45 years, beginning with the early operations of Sauerbruch and of Lexer, as reported by Hoffmeister. The modern treatment of this deformity dates essentially from the paper by Brown in 1939, supported by the subsequent writings of Sweet in 1944, and Lester in 1946. My first operation was performed in January 1947, and the technique described then has been gradually modified. The essential points of the technique as originally described consisted in: (1) removal of all of the deformed costal cartilages for the full length of their deformity; (2) division of the xiphisternal articulation; (3) separation of the intercostal bundles from the sternum; (4) transverse cuneiform osteotomy of the sternum; and (5) maintenance of the sternum in the corrected position by silk sutures without the use of any external fixation. The modified technique, as described in the following paragraphs differs from that first employed principally in the preservation of the perichondrium of the resected costal cartilages and in the tendency to perform the cuneiform osteotomy at a higher level than previously.

OPERATIVE TECHNIQUE

Intratracheal anesthesia is employed and the chest is arched forward slightly by a folded towel placed between the shoulder blades. A midline incision is still used. It is true that occasionally keloids are observed, but the exposure is so much more satisfactorily and easily obtained with the midline incision, and with so much less bleeding, that its continued use was thought justified. In most instances the scars are not objectionable.

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The incision is carried down in the midline from a point on the manubrium, well above the beginning of the declivity, to the midepigastrium. With a periosteal elevator, a flap of skin, subcutaneous fat, and pectoralis major muscle is stripped back to expose the entire area of the deformity. As the muscles are stripped back, the perforating vessels are brought into view and clamped. In children these clamps can be removed presently without the necessity for the use of ligatures. In adults the vessels are coagulated with the electrocautery. The muscles are stripped back in such a way as not to injure the perichondrium. Longitudinal incisions are made through the perichondrium of the involved cartilages and transverse incisions at either end of the longitudinal incisions. If the cut edge of the perichondrium is seized with 2 or 3 small, sharp pointed, curved hemastats placed close together, the perichondrium will begin to separate and can be stripped from the costal cartilage by the use of appropriate elevators. A Joseph's periosteal elevator, such as the plastic surgeons use, is preferred and the tip is kept curved upward toward the perichondrium which is tougher than the cartilage and less likely to be cut inadvertently. The upper flap is usually stripped first and then the lower. Some care must be exercised at the upper edge of the cartilage where the perichondrium generally is so thin that one may perforate it quite readily, passing out into the intercostal muscles. In some instances, it is possible to pass a blunt instrument behind the cartilage, leave the perichondrium intact, and divide the cartilage only at the two ends. In others, it is difficult to strip the perichondrium behind the cartilage. The cartilage is then held up with a Kocher clamp and carefully incised in its midportion until one-half of the cartilage is lifted

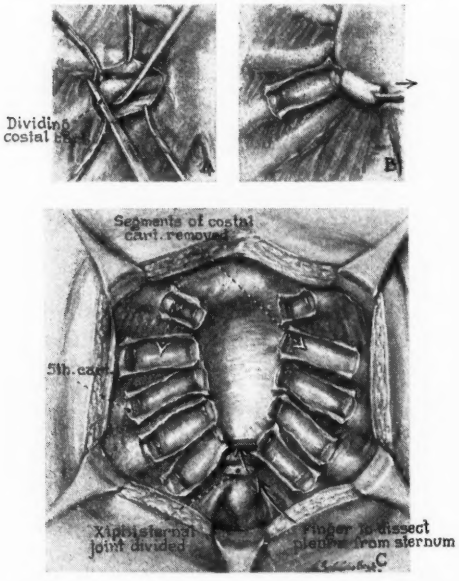

FIG. 2. Each deformed cartilage in turn is removed subperichondrially for the full extent of its deformity. Three to 5 cartilages may be so removed. The xiphoid is divided from the sternum and the finger inserted in the mediastinum (C).

away from the underlying perichondrium. This is stripped away with a Küttner dissector, and the two ends of the cartilage are divided medially and laterally to remove the entire specimen. With a little practice this perichondrial dissection is found to be easily performed, and with rather less effort in infants and children than in adults. All of the deformed cartilages are resected for the full length of their deformity. In small children this may mean as much as 4 or 5 centimeters of the lower cartilages and perhaps only 1½ or 2 centimeters of the upper cartilages. Occasionally as few as 3 cartilages are removed; usually 4, and often 5 on each side are removed. With the sternum held up by a sharp-pointed bone hook, the xiphoid is divided from the sternum and allowed to retract. There is usually one bleeding vessel on either side of the xiphoid which requires clamping. While at times there is a tough fibrous structure on the posterior surface of the xiphisternal area, more often than not this is not present; and, in general, I have not been convinced about the existence of a substernal ligament. The opening made by division of the sternum and xiphoid is enlarged sufficiently to admit one's finger. In infants this may be the little finger. The finger is inserted into the mediastinum, and the pleural reflection is displaced laterally on both sides so that, with traction being made upward on the sternum with the bone hook, it is possible to cut the intercostal bundles away from the sternum on both sides and isolate the sternum as a peninsula, attached only above. If the pleurae are not well stripped away with the finger, it is quite possible to clip a small corner of the pleural reflection. When this happens it is repaired with 1 or 2 fine sutures. At this point, always in adults and older children, and occasionally in small children and in infants, with the finger behind the lowest costal cartilage which has been left intact and which is usually the third costal cartilage, an incision is made with the scalpel through this cartilage about a centimeter from the sternum. When this has been done on either side, a transverse incision is made in the sternal periosteum at the next higher interspace, which is usually the second, and the periosteum is stripped back for a short distance. In children, a small gouge serves amply for the performance of a cuneiform osteotomy, without the necessity for a mallet, and in adults a mallet and osteotome are quite satisfactory. The sternum is steadied during this maneuver by placing an instrument behind it, as shown in Figure 3C. Electric saws are quite unnecessary. At times a very fine curet may be used to remove a little more bone and to deepen the osteotomy incision. Bone chips which are removed in the course of the osteotomy are preserved. At times the gladiolus presents a boat-shaped concavity so that when the upper end is overcorrected, the lower end curves far forward. This defect is then corrected by a second transverse osteotomy in the midportion of the sternum, fracturing the sternum posteriorly. This incision can be held apart and the corrected position maintained, by filling it with the bone chips from the first osteotomy. The upper osteotomy having been completed, the sternum is bent forward and back so that the posterior cortical lamella is fractured until the sternum can be held easily in corrected position. It is held in this corrected, or preferably slightly overcorrected, position by 2 or 3 mattress sutures of heavy braided silk placed through the bone across the incision and tied with a surgeon's knot. Silk is preferred to wire, in the belief that wire may break and that it may be tied

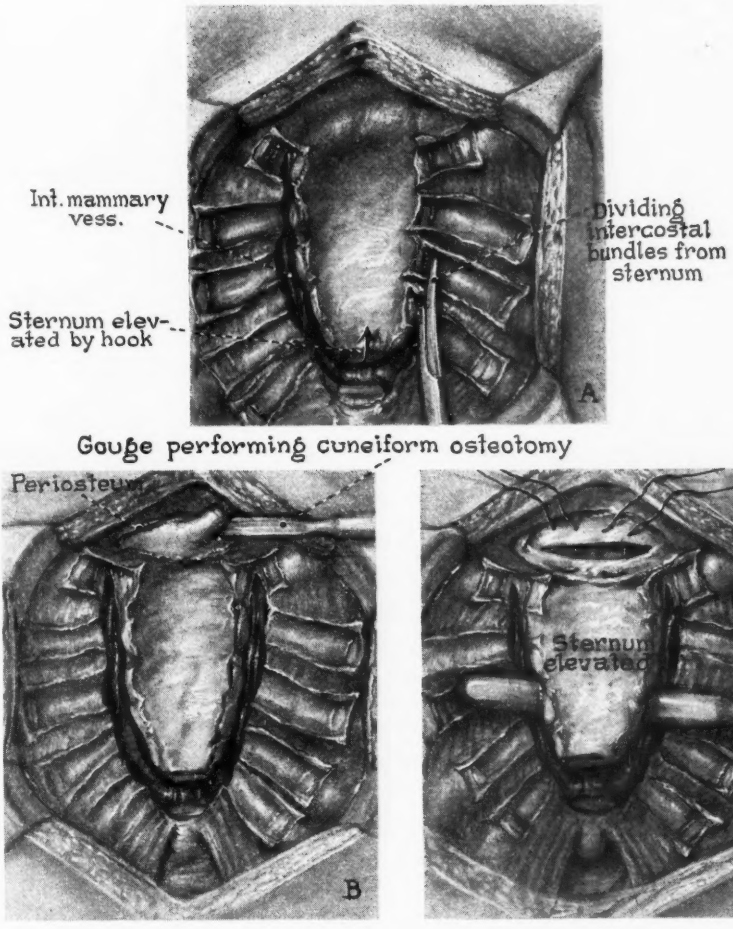

FIG. 3. The sternum being held up by a hook (not shown) after the finger has stripped the pleura back to either side, the intercostal bundles are divided from the sternum. These drawings were made of operation in a 6 month old baby in whom the correction could be adequately achieved in this way. In most instances the next higher costal cartilage, usually the third, is divided with the scalpel close to the sternum, permitting the subsequent sternal osteotomy to be made in the second interspace, rather than the third. The sternal periosteum is incised (B), stripped back, and an osteotomy performed with a gouge and deepened if necessary with osteotomes or curets. The sternum is lifted forward and back until the posterior cortical lamella has been fractured and the sternum easily maintained in corrected position. Stabilized by an instrument passed behind it (C), it is maintained in corrected position by mattress sutures of heavy braided silk placed across the osteotomy.

so tightly as to cut through the bone. Even more dependence is placed on a second row of sutures of No. 0 to 00 silk placed through the periosteum. If the third cartilage has been transected in the manner described, its cut ends are now sutured together in the new position with a heavy silk suture on either side, No. 1 silk in adults and No. 0 silk in children. The xiphoid is not resutured to the sternum since this procedure tends to recreate the deformity. The intercostal bundles are now lifted back and held against the side of the sternum. If they are redundant, as is usually

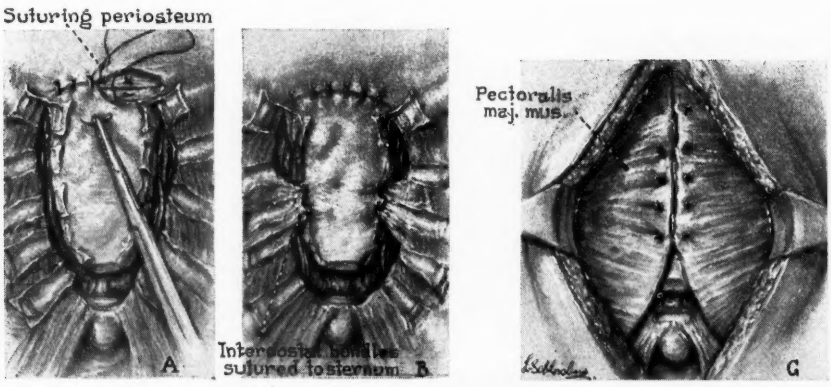

FIG. 4. Sutures of No. 0 or 00 silk in the periosteum further reinforce the maintenance of the sternum in good position (A). In older patients in whom an additional costal cartilage (usually the third) has been divided, this is now resutured with heavy silk, in its corrected position, the medial end more prominent than the lateral end. Any excess of the intercostal bundles is trimmed away and 1 or 2 sutures of No. 0000 silk lightly tack the intercostal bundles to the sternum on either side (B). If this results in any visible tension on the sternum with respiration, the sutures are then cut away and no attempt is made to attach the intercostal bundles. The xiphoid is left separated from the sternum. The pectoralis major muscles are tacked back to the sternal midline (C). The skin is closed with subcutaneous and cutaneous sutures of No. 0000 silk and sprayed with an aerosol plastic dressing. No external fixation of any kind whatsoever is employed.

the case in patients who have had a deep deformity, the redundant tissue is cut away. One or 2 sutures of No. 0000 silk are employed to tack the intercostal bundles lightly to the sternum. If there is any suggestion that tension on the sternum results with each respiration, the sutures are cut away. Substantial experience, with earlier cases, in total excision of the intercostal bundles and perichondrium without any resuturing, has convinced me that it is not important to suture the intercostal bundles back to the sternum, although it does result in a more rapid development of a firm chest wall after operation. The pectoralis major muscles are now sutured to the sternal midline with interrupted sutures of No. 00 silk, and the skin is carefully closed with subcutaneous sutures of No. 0000 silk, and a separate skin closure. An aerosol plastic spray provides the only dressing. I do not employ drains, although a number of other operators do. The operation requires 1½ hours in children, 2 to 2½ hours in adults. Intravenous fluids are always administered during operation but blood transfusion has become the exception. A roentgenogram of the chest is taken immediately after operation to discover any pneumothorax, and in a rare case significant pneumothorax is found and aspirated.

After operation, oxygen is not employed, but in infants some type of apparatus is used to provide moist cold air so that any difficulty from the intratracheal tube may be obviated. Tracheostomy has not been necessary in any case. No restriction is imposed upon activity. Patients are allowed to be up and about as soon as they wish, which is generally in 2 or 3 days. They are discharged from the hospital in 6 to 8 days and advised to avoid strenuous physical activity for 2 more weeks. In perhaps a third of the cases there is an accumulation of serosanguineous fluid in the mediastinum which bulges the wound and requires 1 or 2 aspirations.

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TARSOMETATARSAL FRACTURE DISLOCATIONS

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GREAT FORCE is necessary to dislocate a foot at the tarsometatarsal level. There is severe damage to bone, ligaments, blood vessels, and soft tissue. Failure to achieve prompt and complete reduction leads commonly to gangrene and amputation.

Gissane of Birmingham, England, reported the serious consequences of delay in reducing the dislocation. He treated 3 patients with standard conservative methods for grossly swollen limbs, i.e, elevation, bed rest, cold packs, and splints. Each ended in below-knee amputation. Gangrene supervened because the injury had torn the dorsalis pedis artery at its junction with the plantar arterial arch, and the swelling persisting with the dislocation had occluded the posterior tibial artery. Geckeler of Philadelphia found it impossible to reduce most of the dislocations by closed methods. Consequently he advocated open reduction and fixation by multiple Kirschner wires. Del Sel of Buenos Aires also used open reduction and 1 to 4 Kirschner wires to maintain position. None of these authors described the essentially uniform character of the lesions which permits early closed reduction in uncomplicated cases and automatic selection of those patients who require open removal of an interfering bone fragment.

There are two requirements for treatment. One is an understanding of the injury as an anatomic entity. Knowledge of the anatomic lesions and the basis of their production permits rational and simple treatment for an injury previously regarded as complicated and difficult. The other requirement is an effective means of applying powerful uniform traction (Fig. 3). This can be obtained by using woven wire cylindroids which tighten with tension. The wire traps are placed over the tape protected toes and yoked to a transverse iron bar from which weights may be suspended. The patient is positioned prone with foot projecting beyond table edge. The table provides countertraction and the application of 15 pounds of weight to the bar will restore the foot to length in 5 minutes.

The common denominator of these injuries is that the metatarsus—always the second, third, fourth, and fifth metatarsals with sometimes the first as well—displaces as a unit, a fact easily appreciated when closed reduction is achieved by a mechanical traction device. The reason for this is that the second, third, fourth, and fifth metatarsal bases are bound to each other by transverse ligaments located at both plantar and dorsal aspects (Fig. 1). The plantar ligaments support the arch and are stronger than the dorsal ligaments. There is no ligament between the metatarsals of the great and second toes; instead the 4 lesser metatarsals are fastened primarily to the first cuneiform by obliquely placed plantar and dorsal ligaments. The oblique ligaments are so placed that an abduction force applied to the metatarsus results in rupture or avulsion of their metatarsal insertions and permits lateral dislocation of the forefoot. The great toe metatarsal is secured to the first cuneiform by axially placed ligaments which permit marked abduction before yielding. Great force is necessary to violate these ligamentous attachments.

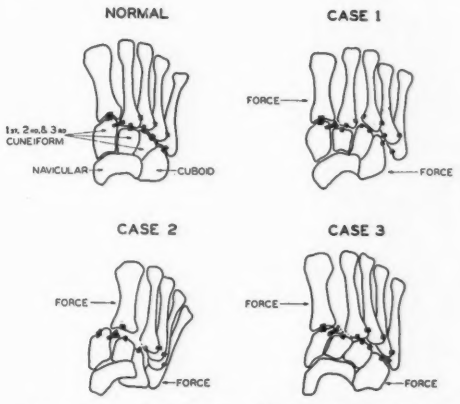

FIG. 1. Schematic diagram of ligaments and their disruptions in the 3 cases presented.

From the Elko Clinic, Elko, Nevada.

FIG. 2.

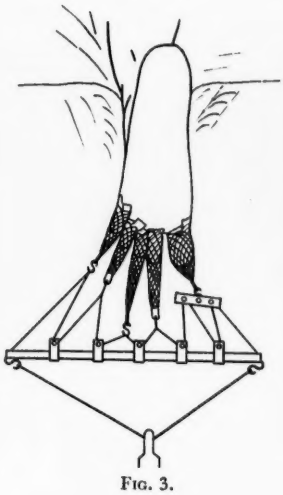

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.

FIG. 7.

FIG. 2. Case 1. Lateral displacement of second, third, fourth, and fifth metatarsals with tiny avulsion fractures at their bases.

FIG. 3. Traction device utilizing wire traps yoked to a traction bar. Note tape protected toes.

FIG. 4. Case 1. Postreduction film.

FIG. 5. Case 2. Typically swollen, shortened, and laterally displaced forefoot of tarsometatarsal fracture dislocation.

FIG. 6. Case 2. Severe five digit lateral dislocation. Note avulsed fragment at mesial base of second metatarsal.

FIG. 7. Case 2. Improved position but incomplete reduction because of bone fragment in cuneiform notch.

FIG. 8.

FIG. 9.

FIG. 8. Case 3. Four digit lateral displacement with bone fragments in the cuneiform notch.
FIG. 9. Case 3. Anatomic position maintained by single Kirschner wire and a cast.

These observations are apparent in the following case reports:

CASE 1. The patient was a 37 year old man whose left foot had been struck by a falling roundhouse door. The forefoot was swollen, shortened, and displaced laterally. Roentgenograms portrayed a fracture dislocation at the tarsometatarsal junction (Fig. 2). The patient was given a spinal anesthesia and traction was applied (Fig. 3). After 5 minutes of steady uniform 15 pound traction, the foot was restored to length. Gentle manual adduction caused sudden reduction which occurred with a loud, sucking snap. This reduction was stable clinically and the roentgenograms confirmed that it was complete (Fig. 4). A short leg plaster cast was applied and left in place for 5 weeks. The foot was supported for 2 additional weeks with Unna boots and elastic bandages. He returned to full work in 9 weeks despite pending litigation against his employer. At last evaluation 9 months after injury, he had a painless foot with no loss of motion.

CASE 2. The patient was a 15 year old boy who injured his right foot in an auto accident. His forefoot showed swelling, shortening, and lateral displacement (Fig. 5). Roentgenograms delineated complete tarsometatarsal fracture dislocation (Fig. 6). The traction device weighted with 15 pounds was applied to the toes of the anesthetized prone patient and a semistable reduction was achieved in approximately 5 minutes. Roentgenograms showed that complete reduction was prevented by a tiny fragment of bone lying at the mesial base of the second metatarsal (Fig. 7). Therefore, a short axial incision was made over the base of the second metatarsal and the fragment removed. A single Kirschner wire was inserted through the lateral aspect of the second metatarsal into the first cuneiform so as to parallel the oblique ligament. This single wire maintained complete reduction. The wound was sutured and a short leg cast was applied for 3 weeks at which time the wire was removed. For 2 more weeks the patient was allowed weight-bearing with a walking cast and then given elastic bandage support for a final 2 weeks. At last evaluation 7 months later, the patient had a painless foot. In the interim this patient ran the 440 yard relay race on the school track team.

CASE 3. A 25 year old man injured his left foot in an auto accident. The characteristic forefoot deformity was present and roentgenograms confirmed a tarsometatarsal fracture dislocation (Fig. 8). As in Case 2, a semistable reduction was obtained with the traction device. The roentgenograms again showed the impeding bone fragment at the cuneiform notch. Surgical removal of the bone fragment which was avulsed from the plantar aspect of the second metatarsal permitted easy reduction which could be held with a single Kirschner wire directed into the cuneiform bone through the lateral side of the second metatarsal (Fig. 9). A short leg cast was applied and the patient returned to his home in another state where the wire was removed in 8 weeks. The patient has not replied to follow-up queries.

SUMMARY

Tarsometatarsal dislocation is an anatomic entity. The involved portion of metatarsus displaces as a unit and its replacement requires sustained even traction. Final reduction is closed or open depending upon the presence, size, and position of the fragment avulsed from the second metatarsal. If surgery is needed to remove the fragment, a single Kirschner wire will stabilize the reduction. Disability time is short and functional result is excellent.

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A NEW NEEDLE AND SAFER METHOD OF ARTERIOGRAPHY

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THE RECENT ADVANCES in cardiovascular surgery have made arteriography an essential part of the preoperative evaluation of the patient. The procedure, however, is sometimes attended by serious complications. The pioneer of translumbar aortography, Reynaldo Dos Santos (1, 2, 3), recognized the dangerous side effects that may complicate the examination and presented his views and recommendations about it. Nevertheless, the early uses of aortography were fraught with discouraging complications, and investigators have directed their efforts toward technical improvements which would make this procedure safe for general use.

The complications of arteriography may be ascribed to mechanical factors or to reaction to the contrast medium. The use of anesthesia may introduce complications of its own. The occurrence of nausea, vomiting, intense sensation of heat, palpitation, and urticaria, has been observed by most investigators. The more serious complications consist of the following: intramural injection and extravasation of the contrast medium; damage to the kidneys; bleeding from the puncture site; thrombosis of the superior or inferior mesenteric arteries with necrosis of the intestines; embolism; paraplegia; and radiation hazard to the angiographer. The first two complications mentioned are the most common.

Extravasation and intramural injections. Extravasation of the contrast medium causes varying degrees of pain, often necessitating the use of strong analgesics. Neuritis has been observed to occur after such extravasation. Although no sequelae have been ascribed to intramural injections of the radiopaque medium, serious dissection into the abdominal aorta has been observed to occur during such injections.

Renal damage. Injection of the contrast medium into the renal artery has led to serious sequelae in many instances. Miller, Wylie, and Hinman, from experiments on dogs, reported that injections under high pressure are responsible for interstitial extravasation of the contrast medium resulting in inflammation, hemorrhage, and fibrosis. Renal fibrosis and atrophy have been observed in patients after injection of the radiopaque solution into the renal artery. This condition may not be clinically evident if only 1 kidney is affected. Indeed, the single fatal complication, in over 140 abdominal aortograms made at City Hospital of Cleveland, was in a 46 year old female patient who had only one functioning kidney. During aortography, the contrast medium, urokon, was injected into the artery supplying the functioning kidney. This was followed by acute hypertension and the development of a tender mass in the right upper quadrant of the abdomen. The only pathologic finding noted at exploration of the abdomen was a hemorrhagic kidney, about 3 to 4 times normal size.

Techniques aiming at reducing the complication of translumbar aortography were introduced. Thus, retrograde abdominal aortography, using the femoral artery as the point of entry, has been developed and popularized. This method entails the danger of perforation of the external iliac artery and the formation of hematomas. Furthermore, it is not applicable in cases of obliterative disease of the terminal aorta. Countercurrent aortography by injecting the femoral artery has also been advocated. The large caliber of the aorta and the rate of blood flow limit the use of this method. Furthermore, it cannot be used in patients whose iliac or femoral arteries are occluded.

Radiation hazard. The importance of the radiation hazard is shown by the recent study of Ritvo, d'Angio, and Rhodes. Under standard arteriographic techniques, the hands alone sustain an average exposure of 300 milliroentgens in femoral arteriography and 6 to 330 microroentgens in translumbar aortography. "The maximum total dose to which the body may be exposed without bodily injury is currently es-

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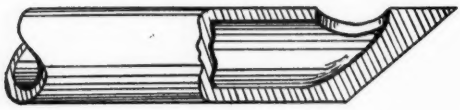

FIG. 1.

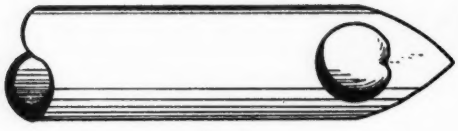

FIG. 2.

FIG. 1. Section of the new needle illustrating the side aperture and the solid tip.

FIG. 2. View of sector at distal arc of aperture.

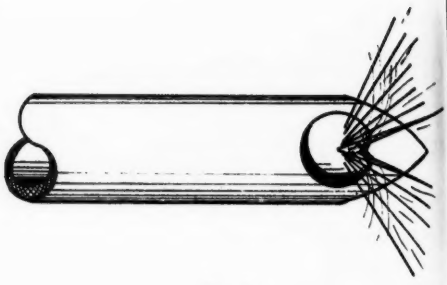

FIG. 3.

FIG. 3. Diagram of the spray produced by the new needle. This was obtained with solutions of different viscosity and density.

tablished at 300 milliroentgens per week." Although the hands can withstand 5 times that dose without harm, the serious damage that may result, if the procedure is often repeated, is obvious. Several devices are currently in use for protecting the examiner against irradiation. This report describes a new needle and a modification of the method employed in arteriography of the major arteries, which it is believed greatly increase the safety of both the patient and the angiographer in this procedure.

NEW NEEDLE

The new aortogram needle (Fig. 1) is of 16 gauge and is 17 centimeters long. The tip is solid and has a short, sharp bevel. The round aperture, with a cross sectional area slightly bigger than that of the lumen, is located on the side opposite the bevel, 2 to 3 millimeters from the tip. In the center of the distal arc of this aperture is a small sector protruding backward (Fig. 2). This sector has been shown not to impede the egress of the contrast medium from the needle, nor does it slow the speed of injection. Figure 4 shows one of the many aortograms obtained with this needle. A similar 18 gauge needle is used for femoral arteriography.

The advantages of the new needle over the standard needle are as follows: (a) The danger from bleeding from the puncture site is lessened. The ordinary needle with its sharp bevel can conceivably cut out a piece of a sclerotic arterial wall during its entry into the diseased artery. In addition to bleeding from the resulting defect in the arterial wall, the "punched out" piece may act as a small embolus. The solid tip of the new needle is less likely to punch its way through a sclerotic arterial wall. (b) The possibility of extraluminal and intramural injections of the contrast medium is nullified. The standard needle will allow back bleeding from the artery under investigation if only part of the tip is intraluminal. The contrast medium may then be forced extra-arterially or intramurally (Fig. 5) thus possibly producing serious dissection of the arterial wall, in addition to the pain and danger of neuritis associated with the extravasation. This is unlikely to occur with the new needle because the side aperture will not allow back bleeding unless it is completely in the lumen of the vessel because of its size and shape; this aperture is round and has a cross-sectional area one-third, at the most, of the oblong aperture of the standard needle. (c) The danger of high pressure injections in the region of the renal arteries is decreased. The sector of the new needle (Fig. 2) acts like an atomizer and reduces a narrow, high pressure stream into a low pressure, wide angle spray. In air, the ordinary 16 gauge needle can be made to eject a vertical column of water over 8 meters high. The new needle does not allow the formation of a column, and the resulting spray does not achieve a height of more than 70 centimeters. It was also demonstrated, by the injection of colored solutions in transparent tubing, that with the standard needle the immediate distance affected by the injection is at least 3 times as long as that affected by the new needle, whether the injections were made into a column of still water or countercurrently against running water. Furthermore, the colored solution diffused into the water medium much faster when in-

FIG. 4.

FIG. 5.

FIG. 4. Abdominal aortogram obtained by using the new needle. The metallic shadows in this picture represent silver clips used in a previous lumbar sympathectomy.

FIG. 5. Abdominal aortogram done with the standard needle illustrates extra-aortic as well as intra-aortic injection of the contrast medium. This happens when the end aperture is partially intraluminal and partially extraluminal.

FIG. 6. Picture illustrating the use of the test dose and showing the tip of the needle to be in the right renal artery. Three milliliters of contrast medium were used.

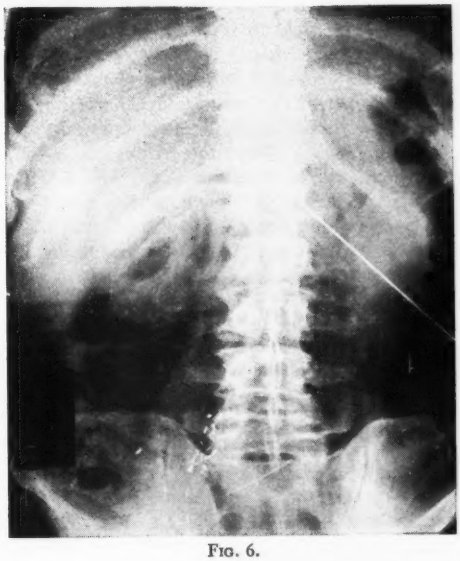

FIG. 6.

jected with the new needle than when t standard needle was used, indicating rapid dilution of the injected medium. (d) The side opening allows directional control of the injected medium more definitely than the terminal aperture of the standard needle and prevents the formation of a jet, which may be directed toward the orifices of aortic branches.

The new needle has been in use at the City Hospital of Cleveland for more than 1 year without complications attributable to it.

Method of arteriography. All arteriograms and aortograms are done percutaneously under 1 per cent procaine local anesthesia. The patients are given an intradermal skin test, using 0.1 milliliter of a 10 per cent solution of iodopyracet. If the result is negative, it is followed by an intravenous sensitivity test using 1.0 cubic centimeter of the same material. Blood pressure, pulse, and respiration are observed and recorded every 15 minutes for 1 hour. On the day of the examination, the patient is allowed no breakfast nor lunch. The premedication consists of 0.5 to 0.75 gram of chloral hydrate, or 100 milligrams of sodium phenobarbital for patients under 50

years of age, about 1½ hours before the procedure. This is followed by 50 to 75 milligrams of demerol hydrochloride, with or without 0.33 milligram of atropine sulfate, about 30 to 45 minutes later. The technique is similar to that used by most investigators. Best results were obtained by using 15 to 25 milliliters of 35 per cent iodopyracet for femoral arteriography and 20 to 25 milliliters of 70 per cent diodrast for abdominal aortography. To this is added 1 milliliter of 2 per cent procaine solution before injection. The 70 per cent solution is kept warm before injection in order to prevent crystallization. Only 2 to 3 milliliters are injected at first and a preliminary film taken. This serves as an additional sensitivity test and also serves to identify the position of the needle in abdominal aortography. If the latter is not in the desired position, viz., renal artery (Fig. 6), superior mesenteric artery, or other branches of the aorta, it is withdrawn and reinserted at a different level before the complete injection is given to the patient.

For protection against unnecessary x-radiation, the following modifications have been introduced: Plastic tubing about 130 centimeters long has been substituted for the short tubing that connects the syringe containing the radiopaque solution to the needle. This permits the examiner to stand behind a lead screen (1/16 inch lead), supplied with a protected glass window, (1/16 inch lead equivalent). The examiner's hands and body are entirely outside the x-ray beam. The exposure resulting from scatter and reflection from the walls of the room is nil, as tested on several occasions by employing a radiation survey meter and film badges to detect radiation exposure.

SUMMARY AND CONCLUSIONS

Arteriography is commonly associated with unpleasant side reactions, such as nausea, vomiting, and palpitation. The judicious use of sensitivity tests for excluding the unusually sensitive patient from the examination, and the addition of 2 per cent procaine to the contrast medium will help to alleviate these undesirable reactions.

Less commonly, arteriography may be attended by serious complications such as extravasation and intramural injection of the contrast medium, kidney damage, bleeding, embolism, paraplegia, and intestinal necrosis. Another complication, frequently overlooked, is the radiation hazard to the angiographer. These complications can be minimized by the following methods: (1) use of the new needle with the side aperture and sector, as described; (2) routine use of an intra-arterial test dose, which serves as an additional sensitivity test, and identification of the position of the needle; (3) use of local rather than general anesthesia; (4) use of smaller doses of iodide solution; and (5) use of long plastic tubing and protective screening to eliminate the radiation hazard.

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GASTROSTOMY TUBES

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THE VALUE of decompression of the stomach and small bowel by means of nasal tubes passed into these organs has been proved in the treatment of paralytic ileus and various types of peritonitis. Nasal tubes can seldom be kept in place for more than 7 to 10 days, and complications often result from their use. Laryngeal ulcerations, which may cause edema and obstruction requiring tracheotomy, and strictures of the esophagus following pressure ulcers caused by tubes are not uncommon. These complications are obvious, sometimes lethal, and are sufficiently startling to cause concern. However, it has been my experience that the less dramatic complications probably result in more deaths and greater morbidity. These complications include rhinitis, sinusitis, and ulceration of the nares and nasal septum. Excessive mucus secretion and the aspiration of mucus plugs result in atelectasis and collapse of the lung, or in bronchopneumonia. The likelihood of aspiration of such plugs is increased by the need for more sedation to lessen the distress caused by the nasal tubes.

Oftentimes, the nasal tube becomes plugged and the patient is seen to vomit around it. Aspiration of vomitus is more apt to occur if a nasal tube is present than if it were not.

Because of my experience with aged and debilitated patients who have a poor cough reflex an attempt was made to establish gastric and intestinal decompression by tubes passed through the gastric wall. From 1951 on, I have used gastrostomy tubes with increasing frequency.

Originally, gastrostomy tubes were used only for those patients who could not tolerate nasal tubes. With increasing experience, gastrostomy tubes have been used more frequently, especially in patients who have seen the freedom from postoperative distress of others in whom these tubes had been used. Up to now such tubes have been used in from 500 to 600 cases.

The tube is often inserted at the beginning of the operation; if it is believed that a patient may need a decompression for more than 24 hours it is generally used. Patients who have any upper respiratory sensitivity, nasal obstruction, or sinusitis, as well as poor risk patients, such as cardiac, asthmatic, obese, or mentally confused patients, are candidates. It is used for decompression after resection and anastomosis of the colon and bowel, and if kept open it will prevent any pressure from distention for long periods, if need be.

A 20 French Levin tube is chosen cut into two pieces (Fig. 1B and C). Holes are cut in the proximal half to provide a second tube. Ordinary 16 to 20 French catheters will serve equally well. Farris has reported success with a Foley catheter type of gastrostomy tube, and Dragstedt uses a similar type of tube for gastric decompression. I place 2 No. 00 silk purse-string sutures in the anterior wall of the stomach at a point where the stomach wall can be fixed easily to the anterior abdominal wall. A small hole is made in the center of the purse-string sutures, and the tube is passed into the stomach for 3 to 4 inches. It is usually directed toward the fundus of the stomach. The purse-string sutures are tied, inverting the edge of the stomach wall about 2 millimeters. If the purse-string suture does not seem to invert the stomach sufficiently, a single suture on one, or both, sides of the tube will give sufficient inversion. A stab wound is made in the skin of the abdominal wall at a previously selected point and a straight hemostat is pushed through the abdominal wall, and the end of the tube is grasped by the hemostat and pulled through the abdominal wall. The stomach wall is fixed to the peritoneum about the tube by 4 or 5 interrupted silk sutures, so that there will be no danger of leakage. A small cutting needle is then used to pass a silk suture through the skin and the tube. This is done to prevent slipping of the tube which is also anchored by adhesive dressings. Usually 2 to 3 ounces of water are injected through the tube to test its patency before the abdomen is closed.

In 2 patients gastrostomy tubes were placed at the time of 3 separate operations. Adhesions have been minimal, and at postoperative fluoroscopic examination the site of the gastrostomy has not caused confusion as to diagnosis.

If a patient has peritonitis, or has had more

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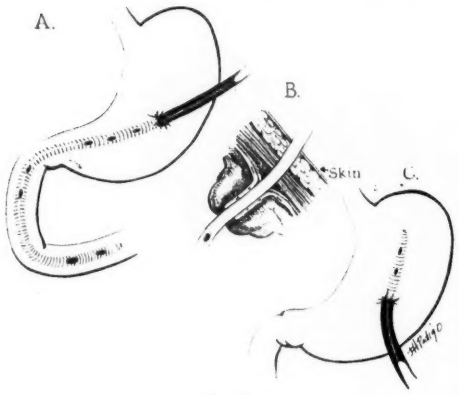

FIG. 1.

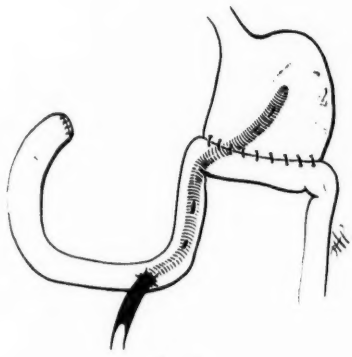

FIG. 2.

FIG. 1. A, The tube is passed into the duodenum and jejunum if the patient has peritonitis or when it is imperative that the small bowel be completely decompressed. B, Inversion of the anterior wall of the stomach about the gastrostomy tube and fixation of the anterior wall of the stomach to the parietal peritoneum are shown. C, The usual placement of a simple gastrostomy tube is illustrated.

FIG. 2. This drawing shows the insertion of a gastrostomy tube through the proximal loop of the jejunum into the stomach during a Billroth II resection. This procedure allows for decompression of both the proximal loop and the stomach. The jejunum is fixed to the abdominal wall, as in Figure 1B.

than 1 resection and anastomosis, or if the duodenum has been opened, the tube is passed into the duodenum or upper jejunum as indicated in Figure 1A. Additional holes are then cut in the part of the tube which will lie in the stomach. In this way, the stomach and small bowel are decompressed simultaneously.

Upon completion of an antecolic Billroth II type of gastric resection, the tube is passed through the anterior wall of the proximal loop, through the anastomosis, and into the stomach (Fig. 2). Additional holes are cut in order to decompress the anterior loop as well as the stomach.

Complications resulting from the use of tubes are rare. Two or 3 patients experienced some bleeding into the stomach, presumably from a small vessel at the site of the gastrostomy incision. None of these, however, needed a transfusion. A ligature is placed on bleeding vessels at the time of operation. Gastric fistulas have not developed in any of the patients after removal of the tube. A few patients have had mild infections in the abdominal wound. In 1 patient, the tube slipped out of place so that part of one of the holes was outside of the stomach. This caused leakage for a few hours, and there was more inflammation than usual. In 1 patient, hiccoughs persisted until the tube was removed. In this case, the edge of the diaphragmatic peritoneum had been fixed to the stomach wall. In the rare instances when a tube does not function, partial removal will usually cause it to work.

Exsanguinating gastric hemorrhages have occurred during the postoperative period in 5 cases after surgery of the bowel. Surgical resection proved these to be acute gastric ulcers, presumably due to stress. In 2, there was some suspicion that the tube may have contributed to the ulcer, possibly because of pressure; however, the incidence of such ulcers has been no greater in those in whom gastrostomy tubes were used than in the other patients.

The tube is removed after 4 to 10 days. It should be kept in place until there is no further likelihood of the need for decompression. These tubes have been used for feeding purposes several times. In 2 desperate cases patients were fed through the tubes for more than 6 weeks.

In a few patients such tubes have been placed without performing a laparotomy. This has been done by making a high left 2 inch paramedian incision under novocain anesthesia. The stomach is partially delivered, the purse-string sutures are

placed, and the tube is inserted. The tube is then brought out through a stab wound at least ½ inch away from the original incision. The stomach is fixed to the peritoneum. When the tube is brought through the stab wound there is seldom infection present, which occurs more frequently if the tube is brought out through the original incision.

A 26 French Pezzer catheter has been used as a feeding gastrostomy tube in 1 patient. It has been in place for 23 months and functions well. A stiff cuff should be placed about the tube with a flange extending into the abdominal wall to prevent the tube from moving on the skin and thus causing irritation. If such a tube should slip out, it can be replaced by a Foley catheter without difficulty, and the bag can be inflated to keep it in place.

CONCLUSION

Gastrostomy tubes for postoperative decompression of the stomach and small bowel have been used for 6 years with ever increasing satisfaction. The greatest advantages are: the freedom from postoperative pulmonary collapse; an average postoperative fever of at least .5 to 1 degree less than that anticipated when nasal tubes are used; the ability to keep tubes in place for long periods for feeding purposes; finally, the ability to lessen fatigue and distress, making it possible to operate on some aged and poor risk patients who could not tolerate a nasal tube for long.

Reviews of New Books

THE AUTHOR of the monograph *Die Therapie des angeborenen Klumpfusses*[1] is extremely well qualified, having had 40 years of experience in the treatment of clubfoot. He had written a treatise on clubfoot in 1917.

In this volume the author discusses the etiology and pathology of clubfoot and describes some of the newer concepts with regard to the etiology.

The embryologic development of the pliable foot may be influenced mechanically but deformities may also be the result of radiation. In animal experiments it was found that these deformities could be inherited —that the early developmental cells could be altered. There is reference to the influence of vitamin deficiencies on the development of the foot, and the role that endocrine disturbance may play in causing deformities. Maternal measles may possibly be the cause of a deformity of the foot.

If the deformity of the foot is the result of a mechanical disturbance from an altered position it is reversible. If it is due to an anomaly, it is also reversible, but not to the extent of establishing a completely normal foot.

The author describes some of the pathologic and anatomic findings in the foot, such as infiltration in the muscles, alteration of the muscle fibers, and abnormal attachments of the posterior tibial and the peroneal muscles. He refers to the contraction of the aponeurosis and ligaments, and the alteration of the bones in relation to each other.

For the most part the deformity is an adaptation to the altered position and, therefore, may be corrected. From this observation follows the importance of early treatment. Like all other authorities the author emphasizes that the earlier the treatment is started the better, and shows that the prognosis with early and persistent treatment is excellent in all cases in which structural defects do not exist.

In the discussion of diagnosis there is emphasis on the importance of analyzing the different segments of the deformity—the adduction, supination, and equinus as well as the varus.

It is important to correct each segment of the deformity gradually. The author's technique is to use a board on the plantar surface of the foot, with felt padding between the board and foot, and with the felt continuing up over the heel. The foot is brought and held in an overcorrected position by means of a flannel-like bandage fastened to the skin with a skin adherent. The next step is to enclose the foot board and bandage with a plaster of paris cast and, at the same time, mold the foot into the overcorrected position. The cast is removed after 1 or 2 days and the bandage is reapplied. It is changed again in a few days. This may be done 4 times before the patient leaves the hospital. This treatment is continued for from 2 to 6 weeks. If there is any tendency to internal rotation a spiral steel spring is fastened between the casts, using the Haglund and Denis Browne principle to bring about external rotation. After full correction is obtained it may be maintained by means of a brace. Abduction and pronation shoes may also be used. The author refers to the techniques of Denis Browne and Kite for taking gradual correction of the foot. In the recalcitrant and recurrent clubfoot, particularly with anatomic defects he advises surgical interference. He may transplant the tendon of Achilles to the lateral side of the os calcis or he may lengthen the tendo achillis. In severe cases he divides the capsule on the medial side of the foot and frees the tight posterior tibial. He lengthens the flexors of the great toe and sometimes the abductors of the great toe. In persistent recurrence he considers the advisability of transference of the anterior tibial laterally. For the neglected cases and cases in older children he may do a multiple wedge operation or arthrodesis with correction by removal of wedges. Reference is made to Hoke's operation and to Brittain's arthrodesis. Very rarely is a derotation operation necessary since the early correction of the clubfoot deformity will tend to derotate the tibia. The principal emphasis in this excellent monograph is on early diagnosis and analysis in these cases and on maintaining the correction until normal muscle balance is re-established.

The format of this book is excellent, and the illustrations are clear and definitive.—*Emil D. W. Hauser.*

THE SECOND EDITION of *The Management of Abdominal Operations*[2] has proved to be a widely favored book, the first having appeared in 1953. Originally, the work was in one large and perhaps unwieldy volume, but the present edition has been divided into two volumes, making it a bit more practical. In a com-

[1]DIE THERAPIE DES ANGEBORENEN KLUMPFUSSES. By Hans Debrunner. 182 pages. 91 illustrations. DM 37.—Stuttgart: Ferdinand Enke Verlag, 1957.

[2]THE MANAGEMENT OF ABDOMINAL OPERATIONS. Edited by Rodney Maingot, F.R.C.S. 2nd ed. Vols. I and II. 1326 pages, 640 illustrations. New York: The Macmillan Co., 1957.

parison of the new edition with the previous one, several differences are obvious. The most impressive is that, although the title of the work is *The Management of Abdominal Operations*, the recent tremendous advances in adjuncts to surgery have made it mandatory to present a thorough background in physiologic principles. Therefore, a goodly portion of the first volume is devoted to preoperative and postoperative factors which might not, in the strictest sense, be considered directly applicable to the "management of the operation," but which are essential for the successful outcome of surgical endeavors today. In an earlier era, as even the edition of 1953 would indicate, surgical textbooks were largely dedicated to demonstration of ways and means of exposing important structures and avoiding anatomic pitfalls.

The first volume of the present edition devotes more than half of its space to strictly physiologic aspects. These include preoperative preparation, anesthesia for abdominal operations, the principles and practice of blood transfusion, and, in a most comprehensive discussion, surgical shock. There is a brief chapter on postoperative care and an excellent summary of knowledge of venous thrombosis and pulmonary embolism. One of the strongest parts of this volume is the chapter on fluid and electrolyte balances. The clear organization and the illustrative photographs, charts, and diagrams do much to clarify these often confusing problems. Chemotherapeutic and antibiotic agents are accorded due discussions, which seem up to date. A separate chapter that deals with the role of vitamins in abdominal surgery is easy to read and supplies a great deal of worthwhile information. Complications of abdominal surgery, such as those which develop in the chest and the genitourinary system, are discussed thoroughly.

The second portion of the first volume is largely a revision of much that appeared in the first edition. In some places there is evidence of rather drastic revision, which is timely. Once again, the illustrations have been brought up to date in most instances and the strict adherence to outline form makes reference easy.

The second volume, somewhat smaller than the first, continues the regional consideration and discussion of the surgery of the various systems contained within the peritoneal cavity.

One of the strongest features of this entire work is the profusion of illustrations; these and an index in each volume make for a most complete reference work.

It is a bit overwhelming to reflect on the tremendous changes which have been made in the brief time since the first edition was published. The neophyte in surgery is called on continually to be familiar with a vast store of information which was not available to the preceding generation. The present edition should go far toward making this information available to him as well as to experienced surgeons who but take the trouble to turn to its pages.—*Edward S. Judd.*

THE READER will find it difficult to set aside the fascinating book entitled *The Century of the Surgeon.*[3] It is an account of the vast developments in surgery that followed the introduction of anesthesia in 1846. The author tells the story through the eyes of one man, Hartmann, who as a medical student witnessed the first public demonstration of ether anesthesia in Boston in 1846. Hartmann spent the rest of his professional life travelling from one important world medical center to another. He recounts personal experiences and conversations with the leaders and contributors who laid the foundations for the development of modern surgery; he describes the slow advances in understanding of sepsis and antisepsis and the identification of bacteria and spores; he glories in the final acceptance of asepsis, in the birth of gastrointestinal surgery, in the gradual recognition of "perityphlitis" as a surgical entity, and finally in the early successes in cardiac suture.

Of special interest to a Boston reviewer is the strange sequel to the account of the first successful public demonstration of ether anesthesia. Morton, the dentist, is depicted as a greedy, egocentric opportunist, who saw in his "preparation" not a boon to mankind, but a means of personal aggrandizement by selfish commercialism. He disguised the smell of ether with perfumes and denied to Warren that ether was the principal pain-relieving agent. He could not patent ether but did patent the method of inhalation through his glass globe. He sought to secure "financial rights" when a patent was issued about 1 month after the public demonstration. He offered licenses to doctors and hospitals for a fee to use his preparation. Only after Morton had encountered difficulty in anesthetizing a patient did he confess that ether was the principal ingredient of his preparation. He hoped thereby to regain the support of the surgeons who suspected him because of his greediness and deceit. The unhappy differences with Wells, who had the idea of anesthesia and was the first to administer nitrous oxide, and Jackson, who suggested to Morton the use of sulfuric ether, are recounted in great detail.

The author gives a vivid picture of the horrors and the triumphs of surgery before the introduction of anesthesia—the rapid but skillful amputations, hemostasis by cautery, the stoic surgeon, the crushing and evacuation of bladder stones, the advanced techniques of reconstructive surgery, such as the "Indian nose," and, finally, the successes in ovariotomy.

The chapter on the development of gastrointestinal surgery is a pathetic account of the futile search by Hartmann for a surgeon who had at that time sufficient experience and confidence to do an operation on the stomach for his wife, dying of a tumor obstructing the pylorus. Billroth had had convincing results in dogs, and success in 1 patient. Others before him were less successful in trying to find the answers to repeated failures. All are now permanently inscribed in the history of gastrointestinal surgery. The time had not come when gastric resection was safe.

The incidents and facts recorded in this volume are well documented. There is an extensive bibliography containing more than 500 references which are annotated in detail, chapter by chapter. The professional reader will be fascinated by the way that facts have been woven into such an interesting story, and the lay reader will find the story and its facts most entertaining and enlightening.—*Bradford Cannon.*

[3] THE CENTURY OF THE SURGEON. By Jürgen Thorwald. 432 pages, 66 illustrations. $5.95. New York: Pantheon Books Inc., 1957.

AN EXCELLENT DESCRIPTION of the operative procedures used on the Head and Neck Service at Memorial Hospital is given in the book entitled *Surgery of Head and Neck Tumors*.[4] It includes the surgical treatment of practically all head and neck tumors, except for those in the brain. This book will be of value to every surgeon engaged in this type of work.

The publishers are to be commended upon the pleasing format and binding. The book is about 400 pages in length, and is divided into two parts.

Part I includes 100 pages of descriptive material concerned with historical procedures, preoperative considerations, technical considerations of surgery in this area, postoperative care, the sequelae of sacrifice of various anatomic structures in the head and neck, general and local complications, and long term cosmetic and functional disabilities following radical surgery of the head and neck.

Part II, 300 pages in length, is presented in "atlas style." It consists of 520 line drawings of various stages of operations on the head and neck, with appended legends. The clear and simple style of these drawings illustrates most of the procedures very well, but is not adequate to demonstrate the complex anatomy encountered in neck dissections. The seven pages devoted to neck dissection do not show the majority of the anatomic structures involved in this operation.

As in most surgical texts, there are strong parts and weak parts. Here, the strong parts are those concerned with destructive surgery and getting rid of the cancer. The weak parts, in the opinion of this reviewer, are those concerned with reconstructive surgery and rehabilitation of the patients. Holes are left in ears, noses are cut off and left off. "One of the greatest drawbacks to bone grafts is their unpredictable tendency towards resorption"; "the expedient of burying a full thickness graft to line the undersurface of such flaps is not practical"; "it is doubtful that any bone graft or metal splint will aid appreciably in restoring the function of mastication in mandibular defects." These and other statements seem to indicate some of the frustrations here. Perhaps the total lack of any photographs of results is another indication.

Many surgeons may believe that more concern with reconstruction in the face and neck will permit more radical destructive surgery in these areas. It may be helpful in securing the patient's forthright permission (without any ambiguous wording), and encourage the surgeon to be more radical in his removal of tissue. This reviewer believes that radical surgery in this area should be done by surgeons who have both good training in general surgery and in reparative and reconstructive surgery, not just one or the other.

One of the strongest sections of this book is the 50 pages on "Operations on the Larynx," which is extremely well done, and may be the best work extant on this subject.

The book is full of sound instruction, based upon a large experience in this field. The statement that "a cervical lymph node should never be excised for biopsy, except as a last resort, and then only after failure of a thorough and repeated search for a primary lesion" can be recommended to every surgeon who operates on the neck.

The widespread change-over from radiation therapy to surgical therapy of these tumors at the Memorial Hospital and elsewhere within recent times reflects the superiority of surgical treatment in such instances. This book is recommended to all surgeons interested in, or undertaking the treatment of head and neck tumors. —*Frank McDowell.*

THE SECOND EDITION of *A Manual of Oral Surgery*[5] by W. Harry Archer has been considerably expanded with the addition of 230 pages and some 350 new photographs of case reports, line drawings, and roentgenograms. This edition, like the well received first edition of 1952, is intended for the use of the oral surgeon, the practicing dentist, and the dental student, presenting a "step-by-step atlas of operative techniques."

The 230 additional pages include chapters on antibiotic therapy by Harold J. Zubrow, and the use of cast splints in the treatment of fractures of the maxilla and mandible by William B. Irby. Many chapters have been rearranged and expanded, among them surgical treatment of cysts of the oral cavity, affections of the salivary glands, surgical treatment of oral nonmalignant tumors, oral malignancies; management of primary lesions, complications associated with oral surgery, radiation therapy for cancer of the oral cavity, fractures of the mandible, maxilla, and facial bones, and treatment of pain in the oral cavity and vicinity. The 350 new photographs are of the same excellent quality as those in the first edition, and the author has added several full color sketches of the anatomy of the head and neck. The numerous additional illustrations of oral cysts, fibro-osteoma, fractures, and many other oral diseases offer further diagnostic aid to the reader. This work is an excellent textbook and reference work of operative techniques in the field of oral surgery. —*Orion H. Stuteville.*

IN AN ERA which produces nuclear powered, rocket, and jet engines, satellites, and possibly space ships that enter and leave the earth's atmosphere with the speed of meteors, the physical properties of metals are of great interest to the engineer. Of more importance to the men who travel in such ships are the physical characteristics of the human skeleton. The application of engineering principles to the study of the stresses and strains which affect the human framework is the subject of the unique work by F. Gaynor Evans.[6]

The author has produced a small and easily readable publication in which he summarizes all that is known about the resistance of bone to physical force. In addition, he has summarized the research of others and himself on the effect of push and pull on osteogenesis, the healing of fractures, and the embryologic development of the skeleton.

[4]SURGERY OF HEAD AND NECK TUMORS. By Hayes Martin, M.D. 430 pages, illustrated. $18.50. New York: Paul B. Hoeber, Inc., 1957.

[5]A MANUAL OF ORAL SURGERY; A STEP-BY-STEP ATLAS OF OPERATIVE TECHNIQUES. By W. Harry Archer, B.S., M.A., D.D.S. 2nd ed. 877 pages, 1400 illustrations. $16.50. Philadelphia and London: W. B. Saunders Co., 1956.

[6]STRESS AND STRAIN IN BONES: THEIR RELATION TO FRACTURES AND OSTEOGENESIS. By F. Gaynor Evans, Ph.D. 245 pages, 42 illustrations. $6.50. Springfield, Ill.: Charles C Thomas, 1957.

He describes in easily, understandable terms the results of experimental investigations of stress-strain phenomena by means of mathematical analysis of sections of bones, photoelastic studies of models of bones, strain-sensitive lacquers, wire-resistant strain gauges, oscilloscopes, and extensometers. A concise glossary of engineering terms and an extensive bibliography are appended.

Of particular interest to the orthopedist and the neurosurgeon is Chapter 9, which describes the "loading characteristics" of the vertebral column and the intervertebral disc. The limits of elasticity and compressibility of the disc are shown, and the effects of laminectomy on the strength of the spinal column are demonstrated and discussed. The orthopedist might wish for another chapter on the loading characteristics of the congenitally abnormal spinal column.

Stress and Strain in Bones adds to our biophysical knowledge of the human skeleton, and it is heartily recommended to all concerned with the care of locomotor disorders. —*C. Roger Sullivan.*

THE TEXTBOOK edited by S. G. Clayton[7] embodies the principles and techniques of obstetrics actually practiced at Queen Charlotte's Maternity Hospital in London, the oldest lying-in hospital in the British Isles. It is designated as a teaching hospital by the National Health Service and in 1953 reported 3,045 in-patient deliveries. The 8 obstetric surgeons to Queen Charlotte's Hospital and 7 other outstanding specialists in related fields collaborated with the editor. Though not specifically stated by the editor it is believed that this book is primarily intended for medical students, but would be a useful reference for anyone practicing obstetrics. The chapters on fetal physiology and the physiology and mechanism of labor are very clear, succinct, and would be helpful as a reference in teaching. The entire book is generously and clearly illustrated. The section on pre-eclampsia and eclampsia includes excellent descriptions and photographs of associated gross and microscopic pathology.

It is obvious that very conservative obstetrics is practiced at Queen Charlotte's Hospital. The prophylactic use of forceps and episiotomy as practiced in many medical centers of the United States is apparently not resorted to at Queen Charlotte's. The management of abortions is also quite different. Curettage for incomplete abortion is suggested only if hemorrhage continues for more than a fortnight in spite of rest, pitocin, and ergotrate. Hot intrauterine douches and ergometrine are advised in treating hemorrhage for incomplete abortion or mole after evacuating the uterus.

The section on hemolytic disease of the newborn, including Rh incompatibility and AB-O disease is very thorough and easily understood. On the contrary, afibrinogenemia is discussed rather sketchily with no specific information about fibrinogen blood levels nor mention of need of giving fibrinogen as such in acute hemorrhage from this cause.

This text is a pleasure to read because of the editor's straightforward style, the clear-cut type on good quality paper, and numerous well selected illustrations. It presents to the student a method of handling nearly all obstetric problems that has proved by experience to be safe. Certain procedures as already mentioned, however, are handled quite differently in England than in many medical centers of the United States. These differences are quite interesting and actually add to the value of the book for the physician practicing in the United States.—*Charlotte H. Kerr.*

THE BOOK entitled *Textbook of Urology*[8] is an excellent, practical guidebook for the student and clinician. Dr. Marshall has drawn from his large clinical experience at New York Hospital and his annual teaching of undergraduate medical students at Cornell to assemble this unique work on the diagnosis and treatment of disorders of the genitourinary tract. The contents are listed under 19 separate headings which do not follow the traditional order. I think this is a great improvement from the students' point of view. Marshall states that the book was developed as the result of 20 formal lectures presented to third year medical students. For this purpose, the over-all presentation is ideally suited. Recent third year teaching in most schools has tended toward providing the student with a simple, but complete text or outline so that the available hourly periods could be used for demonstrations and clinics. The need for complete and careful urologic study to supplement the systemic examination is clearly outlined. Chapters of special merit are those dealing with obstructive uropathy and infection, the neurogenic bladder, male infertility, and impotence. This work can be highly recommended for students and will be profitable for the general practitioner of medicine and surgery. —*Vincent J. O'Conor.*

FOR 25 YEARS, Illingworth and Dick's *A Textbook of Surgical Pathology*[9] has continued through 6 editions as an expert and honored guide to a field that ever demands more extended coverage. The seventh edition, still maintained within almost the same size-confines as the first, continues to provide senior and graduate students with an account of the pathology of surgical diseases, certain aspects of which are but lightly treated in the heavier tomes of general pathology.

Continuing as fundamental teaching principles are the embryologic and anatomic approaches to the understanding of pathologic processes involving various tissues and organs. In these aspects the textbook excels. The chapters on infections, specific and nonspecific, have been revised in keeping with the advances made in the chemotherapeutic and antibiotic fields. Throughout the various sections the authors have emphasized the newly discovered roles of the adrenal and pituitary hormones in the light of their metabolic effects on disease processes. The chapters on thoracic and cardiovascular diseases have received

[7]THE QUEEN CHARLOTTE'S TEXT-BOOK OF OBSTETRICS. Edited by S. G. Clayton. 9th ed. 547 pages, 246 illustrations. London: J. & A. Churchill, Ltd.; Boston: Little, Brown & Co. 1957.

[8]TEXTBOOK OF UROLOGY. By Victor F. Marshall, M.D., F.A.C.S. 268 pages, 56 illustrations. $5.50. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros., 1956.

[9]A TEXTBOOK OF SURGICAL PATHOLOGY. By Charles F. W. Illingworth, C.B.E., M.D., Ch.M., F.R.C.S. (Ed.), and Bruce M. Dick, M.B., F.R.C.S. (Ed.). 7th ed. 730 pages, 322 illustrations. $14.00. Boston: Little, Brown & Co., 1957; London: J. & A. Churchill, Ltd., 1956.

expanded treatment consistent with surgical advances made in these particular fields. In tumor pathology, carcinoids, tibial adamantinomas, and Hürthle cell tumors have been placed in their new perspectives. An entirely new chapter has been added on the preservation and transplantation of tissues. In these and many other regards, the seventh edition is an improvement over its predecessors.

As a surgical pathologist, the reviewer was disappointed at failing to find any mention of fresh-tissue methods of diagnosis, a source of help for which every surgeon has a right to dream. As a cytologist he was more than surprised that a field of science entering its teen-age period was accorded no reference. He would agree with those gynecologists who object to use of the term "dysgerminoma" (p. 713) as a synonym for "arrhenoblastoma"; and he would wonder with his urologic colleagues at the propriety of accepting the implantation theory for the spread of transitional cell carcinomas.

These, however, are minor objections in the light of the over-all character of the textbook—an attempt by very experienced surgeons to portray for their young successors the diagnostic aspects of lesions occurring in surgical patients. For this reviewer, Illingworth and Dick was one of his biblical books in medical school days. He continues to recommend it highly.

—*Malcolm B. Dockerty.*

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

Consciousness and the Chemical Environment of the Brain. Report of the Twenty-fifth Ross Pediatric Research Conference. 109 pages, illustrated. Columbus: Ross Laboratories, 1958.

Heart Disease and Pregnancy: Physiology and Management. By C. Sidney Burwell, M.D., and James Metcalfe, M.D. 338 pages, illustrated. Boston and Toronto: Little, Brown & Co., 1958.

Aortography; its Application in Urological and Some Other Conditions. By W. Barr Stirling, Ch.M., F.R.C.S.(Ed.). 292 pages, illustrated. $10.00. Edinburgh and London: E. & S. Livingstone Ltd., Baltimore: Williams & Wilkins Co., 1957.

The Respiratory Muscles and the Mechanics of Breathing. By E. J. Moran Campbell, M.D., Ph.D., B.Sc.(Lond.), M.R.C.P.(Lond.). 131 pages, illustrated. $4.25. Chicago: Year Book Publishers, 1958.

The Clinical Application of Hormone Assay. By John A. Loraine, M.B., Ph.D. (Ed.), M.R.C.P.(Ed.). 368 pages, illustrated. $7.00. Edinburgh and London: E. & S. Livingstone Ltd., Baltimore: The Williams & Wilkins Co., 1958.

New England Journal of Medicine Medical Progress Series. Erythroblastosis Fetalis including Exchange Transfusion Technic. By Fred H. Allen, Jr., M.D., and Louis K. Diamond, M.D. 143 pages, illustrated. $4.00. Boston and Toronto: Little, Brown & Co. 1958.

The Essence of Surgery. By C. Stuart Welch, M.S., M.D., Ph.D., and Samuel R. Powers, Jr., A.B., M.D., M.Sc.D. 320 pages, 50 illustrations. $7.00. Philadelphia and London: W. B. Saunders Co., 1958.

Gastro-Duodenal Ulcer; Physio-Pathology, Pathogenesis and Treatment. By J. Jacques Spira. 549 pages. $14.70. London: Butterworth & Co., Ltd., 1956.

Operative Surgery. Edited by Charles Rob, M.C., M. Chir., F.R.C.S., and Rodney Smith, M.S., F.R.C.S. Vol. VI.—Hand, Amputations, Plastic Surgery, and Gynecology and Obstetrics. 127 pages, illustrated. London: Butterworth & Co., Ltd., 1958.

Archivio "Putti" di chirurgia degli organi di movimento. Bibliografia 1955. Directed by O. Scaglietti. Edited by L. Gui. Vol. IX. Scientifiche dell "Istituto Ortopedico Toscano," 1957.

General Pathology; Based on Lectures Delivered at the Sir William Dunn School of Pathology, University of Oxford. Edited by Sir Howard Florey. 2nd ed. 932 pages, illustrated. $16.00. Philadelphia and London: W. B. Saunders Co., 1958.

How to Write Scientific and Technical Papers. By Sam F. Trelease. 185 pages, not illustrated. $3.25. Baltimore: The Williams & Wilkins Co., 1958.

Tracheotomy; a Clinical and Experimental Study. By Thomas G. Nelson. 111 pages, illustrated. $3.75. Baltimore: The Williams & Wilkins Co., 1958.

New and Nonofficial Drugs; Containing Descriptions of Therapeutic, Prophylactic and Diagnostic agents. Evaluated by the Council on Drugs of the American Medical Association, 1958. 645 pages, not illustrated. Philadelphia and Montreal: J. B. Lippincott Co., 1958.

Recent Advances in Obstetrics and Gynaecology. By Aleck W. Bourne, M.B., B.Ch.(Camb.), F.R.C.S.(Eng.), F.R.C.O.G., and Leslie H. Williams, M.D., M.S.(Lond.), F.R.C.S.(Eng.), F.R.C.O.G. 9th ed. 348 pages, 78 illustrations. $8.00. Boston: Little, Brown & Co. 1958.

The Story Behind the Word; Some Interesting Origins of Medical Terms. By Harry Wain, M.D. 342 pages, not illustrated. $8.50. Springfield, Ill.: Charles C Thomas, 1958.

Chirurgia Demolitiva del Fegato. By Vittorio Pettinari. 230 pages, illustrated. Milan: Idos; Padova: Riccardo Zannoni & F°., 1958.

Jacksonian Prize Essay Royal College of Surgeons 1956; a Contribution to the Study of Portal Hypertension. By Alan Henderson Hunt, D.M., M.Ch., F.R.C.S. 230 pages, illustrated. $8.50. Edinburgh and London: E. & S. Livingstone Ltd.; Baltimore; Williams & Wilkins Co., 1958.

Extracorporeal Circulation. Edited by J. Garrott Allen. Assisted by Francis D. Moore, Andrew G. Morrow, and Henry Swan II. 518 pages, illustrated. $7.50. Springfield, Ill.: Charles C Thomas, 1958.

Endocrine Pathology of the Ovary. By John McLean Morris, M.D., and Robert E. Scully, M.D. 151 pages, 75 illustrations. $8.50. St. Louis: The C. V. Mosby Co., 1958.

Vitallium Mould Arthroplasty for Osteoarthritis of the Hip Joint; a Study of the Ability of the Method to Create a New Joint in an Anatomical-Physiological and in a Clinical Sense. By Arnt Jakobsen, M.D. 277 pages, illustrated. $9.00. New York: The Macmillan Co., 1958.